

# DEPARTMENT OF DEFENSE



## COMPREHENSIVE CLINICAL EVALUATION PROGRAM

FOR

PERSIAN GULF WAR VETERANS

*CCEP Report on 18,598 Participants*

April 2, 1996

DISTRIBUTION STATEMENT A

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# TABLE OF CONTENTS

<b>TABLES</b> .....	iv
<b>FIGURES</b> .....	vi
<b>EXECUTIVE SUMMARY</b> .....	1
<b>BACKGROUND</b> .....	5
<b>Introduction</b> .....	5
<b>Potential Health Risks Associated with Persian Gulf Deployment</b> .....	6
<b>DoD Actions and Initiatives</b> .....	6
CCEP Specialized Care Center (SCC) .....	10
Institute of Medicine Review.....	10
Persian Gulf Veterans' Coordinating Board.....	11
<b>What's New in This Report</b> .....	12
<b>METHODS</b> .....	13
<b>RESULTS</b> .....	15
<b>Program Status</b> .....	15
<b>Demographics</b> .....	16
<b>Self-Reported Exposures</b> .....	18
<b>Physician-Elicited Symptoms</b> .....	19
<b>CCEP Diagnoses</b> .....	22
Examination of the Top Three Primary Diagnostic Categories.....	26
Distribution of Primary Diagnosis Based upon Chief Complaint .....	31
Frequency of Secondary Diagnoses Given a Primary Diagnosis .....	34
<b>Unit Identification Codes (UICs)</b> .....	36
<b>Disability Indicators</b> .....	41
Self-Reported Lost Workdays .....	41
DoD's Physical Evaluation Board Experience .....	43
<b>Diagnoses among Family Members</b> .....	44
Spouses .....	44
Children .....	45

Self-Reported Reproductive Events and Conditions .....	46
Satisfaction Rates of Participants .....	47
Comparison of Diagnoses in CCEP to NAMCS .....	48
<b>DISCUSSION</b> .....	51
Limitations in Interpreting Results of the CCEP .....	51
Demographics .....	52
CCEP Participation Rates and Unit Identification Codes (UICs) .....	53
Potential Exposure(s) .....	53
Symptoms .....	58
Diagnoses .....	60
Psychological Conditions .....	60
Musculoskeletal Diseases .....	62
Symptoms, Signs, and Ill-Defined Conditions .....	63
Characterization of Individuals with More Than One Diagnosis .....	63
NAMCS Comparison .....	64
Physicians' Review .....	66
Respiratory Disorders .....	66
Dermatologic Conditions .....	67
Neurological Diagnoses .....	68
Infectious Disease .....	68
Sleep Disturbances .....	70
Memory Complaints .....	71
Disability .....	72
Reproductive Outcomes .....	73
Individual and Group Response to Environmental Factors Contributing to Health Consequences Among CCEP Participants .....	75
Discussion of Evidence For and Against a Single, Unique Syndrome .....	78
Causality and Health Outcomes .....	82
Research Efforts .....	83
<b>CONCLUSIONS</b> .....	85

Table 18. The Proportion of Secondary Diagnoses Given a Primary Diagnosis of Respiratory .....	35
Table 19. Descriptive Characteristics of Units in the Lowest and Highest CCEP Participation Groups.....	37
Table 20. Self-Reported Exposure History for Members of Units with Lowest and Highest CCEP Participation Rates .....	38
Table 21. Symptom Frequency for Members of Units with Lowest and Highest CCEP Participation Rates .....	39
Table 22. Frequency Distribution Comparison of Primary Diagnoses for Members of Units with Lowest and Highest CCEP Participation Rates .....	40
Table 23. Frequency Distribution of Any Diagnoses for Members of Units with Lowest and Highest CCEP Participation Rates.....	41
Table 24. Workdays Lost to Illness in Past 90 Days by Primary Diagnosis.....	42
Table 25. Comparison of PEB Experience for Non-CCEP PGW Veterans and CCEP Participants.....	43
Table 26. Distribution of Primary Diagnoses and Any Diagnosis for Spouses.....	44
Table 27. Frequency Distribution of Primary Diagnosis for CCEP Children of Persian Gulf War Veterans.....	45
Table 28. Frequency of Self-Reported Reproductive Events and Conditions .....	46
Table 29. Frequency of Primary Diagnoses for CCEP and NAMCS, by Sex, for Subjects Aged 20-40 Years .....	49
Table 30. Most Frequent Psychological Conditions among CCEP Participants .....	61

# FIGURES

Figure 1.	Disposition of CCEP Participants as of December 6, 1995.....	15
Figure 2.	Frequency Distribution of Diagnoses among 18,075 CCEP Participants .....	24
Figure 3.	Distribution of Primary Diagnoses Based upon Chief Complaint.....	32
Figure 4.	Participants' Satisfaction (N=12,283) .....	47
Figure 5.	Common Symptom Prevalence as Reported in Three Studies of Outpatient Practice in the United States, as Compared with CCEP .....	59

# TABLES

Table 1.	Demographic Characteristics of CCEP Participants and Persian Gulf War Participants.....	17
Table 2.	Self-Reported Exposure History .....	19
Table 3.	Symptom Frequency for CCEP Participants.....	20
Table 4.	Frequency of Date of Onset by Symptom.....	21
Table 5.	Primary Diagnoses Occurring in Greater Than 1% of CCEP Participants .....	22
Table 6.	Frequency Distribution of Primary Diagnoses and Any Diagnoses .....	23
Table 7.	Frequency of Primary Diagnoses Over Time .....	25
Table 8.	Number and Percent of Primary Diagnoses of Psychological Conditions (ICD-9-CM Codes 290-319).....	26
Table 9.	Number and Percent of Primary Diagnoses of Symptoms, Signs, and Ill-Defined Conditions (ICD-9-CM Codes 780-799) .....	27
Table 10.	Number and Percent of Primary Diagnoses of Musculoskeletal Conditions (ICD-9-CM Categories 710-739).....	28
Table 11.	Frequency of Most Prevalent Primary Diagnoses by Age Group.....	29
Table 12.	Frequency of Most Prevalent Primary Diagnoses by Sex.....	29
Table 13.	Frequency of Most Prevalent Primary Diagnoses by Military Branch.....	30
Table 14.	52 Cases of Malignant Neoplasms by Sex in CCEP Participants.....	31
Table 15.	The Proportion of Secondary Diagnoses Given a Primary Diagnosis of Psychological .....	34
Table 16.	The Proportion of Secondary Diagnoses Given a Primary Diagnosis of Symptoms, Signs, and Ill-Defined Conditions .....	35
Table 17.	The Proportion of Secondary Diagnoses Given a Primary Diagnosis of Musculoskeletal .....	35

# APPENDICES

<b>APPENDIX A: RELATED DoD ACTIVITIES .....</b>	<b>89</b>
<b>Persian Gulf “Declassification and Investigation” Effort .....</b>	<b>89</b>
<b>DoD Research Efforts .....</b>	<b>90</b>
<b>APPENDIX B: METHODS .....</b>	<b>95</b>
<b>Clinical Evaluation Process .....</b>	<b>95</b>
<b>Institute of Medicine (IOM) .....</b>	<b>96</b>
<b>Data Management Process .....</b>	<b>97</b>
<b>Quality Control Procedures .....</b>	<b>97</b>
<b>Analytic Approach .....</b>	<b>98</b>
Demographics .....	98
Self-Reported Exposures .....	99
Physician-Elicited Symptoms .....	99
Diagnoses .....	99
Reproductive Outcomes .....	100
Unit Identification Codes .....	101
Self-Reported Lost Workdays .....	102
Physical Evaluation Boards .....	102
National Ambulatory Medical Care Survey .....	102
Program Satisfaction .....	102
<b>Statistical Analysis .....</b>	<b>103</b>
<b>APPENDIX C: ICD-9-CM CODE DISTRIBUTION (Primary Diagnosis) .....</b>	<b>105</b>
<b>APPENDIX D: GLOSSARY OF ACRONYMS .....</b>	<b>111</b>
<b>REFERENCES .....</b>	<b>113</b>

# EXECUTIVE SUMMARY

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Approximately 697,000 U.S. service members deployed to the Persian Gulf in 1990/1991 for Operations Desert Shield/Storm (ODS/S). The vast majority of troops returned from this large deployment healthy. In response to Gulf War veterans' concerns about the potential health effects of service in ODS/S, the Departments of Defense (DoD) and Veterans Affairs (VA) developed similar, clinical evaluation programs to provide them care and to understand the nature of their illnesses. The DoD Comprehensive Clinical Evaluation Program (CCEP) provides a systematic, in-depth medical evaluation for DoD beneficiaries (Persian Gulf War veterans now on active duty or retired; members of the full-time National Guard who are Persian Gulf veterans; Persian Gulf War veterans who are members of the Ready Reserve/Individual Ready Reserve/Standby Reserve/Reserve who are placed on orders by their units; and eligible family members of such personnel) who are experiencing illnesses that may be related to their service in the Persian Gulf. As of early December 1995, more than 27,000 individuals had enrolled in the program. Approximately 21,000 of these participants requested an examination of which 18,598 had completed the evaluation process and had the information about their health verified and entered into the CCEP database.

This descriptive case series report summarizes the diagnostic results of over 18,000 systematic clinical evaluations completed through the CCEP. The CCEP was designed primarily as a clinical rather than a research program. Self-selection of patients, recall bias, inability to validate self-reported exposures, and the lack of an appropriate comparison or control group limit the ability to generalize the CCEP findings to other Persian Gulf veterans. However, the large size of the CCEP cohort and the thoroughness of the CCEP examinations provide considerable clinical insight towards understanding the nature of these veterans' illnesses and health concerns. Ongoing and planned epidemiologic studies by the Department of Defense, Veterans Affairs, and Health and Human Services which involve control/comparison populations, will characterize further any health consequences of the Persian Gulf War.

Based on the evaluation of 18,598 participants, our findings include:

- CCEP participants report a wide variety of symptoms spanning multiple organ systems in no consistent, clinically apparent pattern. In the clinical literature, only a limited number of studies of symptoms of patients in other clinical and survey settings have been published. These other study populations are not completely analogous to the CCEP population, since they generally involve older patients and more women than found in the CCEP. However, these studies of outpatient practice and the general U.S. population suggest that the types of symptoms being reported in the CCEP are not unique and are similar in nature to those seen in other groups of patients.
- Symptoms such as fatigue, joint pain, headache, or sleep disturbances are common among CCEP participants. Published studies involving patients with these types of generalized symptoms have shown that 20-75% of them lack a clear-cut or discrete physical explanation or “cause” after a thorough medical evaluation. Similarly, it is likely that some CCEP participants may also lack a discrete physical explanation for their generalized symptoms.
- The distribution of primary diagnoses seen in CCEP participants spans many different organ systems as categorized according to the International Classification of Diseases-Ninth Revision, Clinical Modification (ICD-9-CM). However, over half (65%) of the primary diagnoses of CCEP participants are concentrated in four diagnostic groups: “Psychological Conditions,” “Symptoms, Signs, Ill-Defined Conditions,” “Musculoskeletal and Connective Tissue Diseases” and “Healthy” (V65.5).
- Gulf War veterans who have participated in the CCEP are experiencing real symptoms and illnesses with real consequences, although the vast majority of participants are apparently able to function in their jobs. Severe disability, measured in terms of reported lost workdays, is not a major characteristic of CCEP participants. Relatively few CCEP participants report missing work because of illness or injury during the 90 days prior to

their initial evaluation. Determination of the extent to which the CCEP disability experience reflects the overall disability experience of Persian Gulf veterans is limited by the fact that many Persian Gulf War veterans are no longer on active duty.

- Comparisons of CCEP participants with patients in outpatient medical settings are limited because of differences in patient populations. However, some existing clinical studies provide a context in which to consider the following CCEP findings.
  - The most common psychological conditions found in CCEP participants are: tension headache; nonspecific, mild, or stress-related anxiety and/or depression; and posttraumatic stress disorder (PTSD). The prevalence of psychological diagnoses among CCEP participants may be higher than that observed in other patients seen in general medical practice.
  - CCEP diagnoses include a group of common medical conditions not classified elsewhere in the ICD-9-CM coding system (e.g., sleep apneas), generalized symptoms, abnormal laboratory tests, and nonspecific physical findings. These diagnoses, which are categorized as “Symptoms, Signs and Ill-Defined Conditions” according to the ICD-9-CM coding system, may occur more frequently in the CCEP than among patients seen in general medical practice.
  - Musculoskeletal and connective tissue diseases (joint pain, osteoarthritis, backache) are common diagnoses seen in CCEP participants. These conditions appear to occur more frequently in the CCEP population than they do in patients seen in general medical practice.
- The evaluation of reproductive risks to men and women from environmental exposures is a complex and emotional issue. Some CCEP participants self-report experiencing adverse reproductive events since the Gulf War. However, these reports have not been validated review of medical record or other sources of information. Reproductive studies of other groups of Persian Gulf veterans, which have involved review of medical records

and related databases, have to date found no evidence of increased reproductive problems. Clearly this is an important issue, which the Department will study further.

- To date, there is no clinical evidence for a previously unknown, serious illness or “syndrome” among Persian Gulf veterans participating in the CCEP. A unique illness or syndrome among Persian Gulf veterans evaluated through the CCEP, capable of causing serious impairment in a high proportion of veterans at risk, would probably be detectable in the population of 18,598 patients. However, an unknown illness or a syndrome that was mild or affected only a small proportion of veterans at risk might not be detectable in a case series, no matter how large.

DoD will continue to provide comprehensive high quality health care to eligible Persian Gulf veterans and their family members and will continue its efforts to understand any health consequences of service in the Persian Gulf War. The Department is committed to a continuing exchange of relevant information with other government agencies, researchers, and Gulf War veterans to further understand this important public health issue.

# BACKGROUND

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## Introduction

Iraq invaded Kuwait on August 2, 1990. Subsequent implementation of Operation Desert Shield occurred at a rapid pace, and approximately 697,000 U.S. service members were deployed to the Persian Gulf region over the next five months. Fortunately, hostilities did not begin immediately, and medical personnel had an opportunity to assess medical threats, formulate effective surveillance efforts, and design preventive programs to keep non-battle morbidity and mortality at the lowest possible levels.<sup>1,2</sup> By the time Operation Desert Storm began in January 1991, the soldiers, sailors, airmen, and marines in this operation were, in many respects, more closely monitored for the emergence of medical problems, and better protected from environmental threats, than service members in any previous campaign. These measures were successful; the Gulf War had a lower disease non-battle injury (DNBI) rate than any major conflict in U.S. history.<sup>3,4</sup>

Since Operations Desert Shield/Storm (ODS/S), some Gulf War veterans have reported persistent symptoms that they believe are related to their experience in the Persian Gulf War. These symptoms most commonly included fatigue, joint pain, sleep problems, loss of memory, rash, or headache. In response to veterans' concerns about their health following ODS/S, the Departments of Defense (DoD) and Veterans Affairs (VA) developed similar comprehensive clinical evaluation programs. As of early December 1995, the DoD had enrolled over 27,000 participants eligible for DoD health care in the Comprehensive Clinical Evaluation Program (CCEP).

In December 1994, the DoD issued its preliminary status report on the first 1,000 patients to complete the CCEP.<sup>5</sup> Since that report, the Department has continued an aggressive outreach

effort to provide evaluation and care to veterans who are experiencing illnesses that they feel may be related to their service in the Persian Gulf. On March 10, 1995, the DoD provided updates of the results of 2,076 medical evaluations accomplished through the CCEP<sup>6</sup> and in August 1995 presented a report on 10,020 participants.<sup>7</sup> This report summarizes program activities through December 6, 1995, and includes the clinical findings from 18,598 participants who have requested and completed their CCEP evaluations. Additionally, this report updates information provided in previous reports and presents recent results from the CCEP in order to further describe the clinical characteristics of CCEP participants.

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## **Potential Health Risks Associated with Persian Gulf Deployment**

A number of questions have arisen about the possible impact of certain environmental exposures and preventive medicine measures on service members during ODS/S. To better understand the health concerns among Gulf War veterans and provide the most effective treatments of their illnesses, a review of potential health risks associated with service in the Persian Gulf is necessary. These risks include physical and psychological stress, possible reactions to prophylactic drugs and vaccines, infectious diseases, and exposures to environmental hazards.<sup>8</sup> In addition, there has been a concern among some veterans that chemical and biological weapons may be associated with some of their symptoms. As observed in studies of veterans of other wars, readjustment disorders and posttraumatic stress disorder (PTSD) have been common problems among Persian Gulf veterans.<sup>9,10,11,12,13</sup>

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## **DoD Actions and Initiatives**

The DoD began to assess the health consequences of the Persian Gulf War while troops were still deployed in the Gulf region. As early as February 1991 a medical workshop convened in Dayton, Ohio, to consider the medical effects that might occur among troops exposed to crude oil released from damaged wells during the course of Operation Desert Storm.<sup>14</sup> In May 1991 the DoD deployed a team of physicians, scientists, and engineers to the Persian Gulf region to

establish monitoring stations in both Kuwait and Saudi Arabia to assess the potential environmental health risks to service members. The Kuwaiti Oil Fire Health Effects Working Group was formed in August 1991 to provide technical oversight of the Department's efforts to conduct a comprehensive health risk assessment of effects of exposures to smoke from the Kuwaiti oil well fires.<sup>15</sup> Additionally, an Expert Panel on Petroleum Toxicity met in June 1991 at the Uniformed Services University of Health Sciences (USUHS) to review and discuss scientific information pertaining to health effects that might be expected to result from exposure to the oil well fires.<sup>16</sup>

While these scientific/technical reviews were in progress, the Department was also conducting field investigations of groups of veterans with health complaints. During 1992 "clusters" of military personnel presented with nonspecific symptoms they attributed to their Gulf War service, which resulted in two field investigations. The Army investigated one such cluster among members of the 123rd Army Reserve Command in Indiana. In April 1992 the investigators concluded that the paucity of abnormal physical or laboratory findings, the types of symptoms reported, the association of onset of symptoms with redeployment, and the results of the psychiatric evaluation suggested that many of the symptoms were likely to be stress-related.<sup>17</sup> The Navy conducted a similar investigation of a reserve Seabee battalion (Naval Reserve Mobile Construction Battalion 24) from November 1993 to October 1994. Many members of this unit complained of symptoms that they believed were related to their service in the Persian Gulf. Although investigators confirmed that a significant number of individuals had experienced an array of nonspecific symptoms since returning from the Gulf, no common syndrome or diagnosis was identified in this group of veterans.<sup>18</sup>

Initially, the three Services began to identify military members with possible Gulf War-related medical conditions through routine health surveillance programs designed to track reportable diseases. In August 1992 the Army Surgeon General directed clinicians to identify individuals with medical conditions that might be related to service in the Persian Gulf. In October 1992 the Assistant Secretary of Defense (Health Affairs) requested the Services to provide reports of the numbers of personnel who had been evaluated for complaints attributed to service in the Persian

Gulf. By April 1993 a total of 264 individuals were reported by the three Services. The diseases reported were distributed across 62 different categories. By January 1994 the Services had identified approximately 400 individuals with Gulf War-related health complaints and/or medical problems.

Concurrent with clinical activities and preliminary epidemiological field investigations, the Department organized several independent reviews of health issues involving Persian Gulf veterans. In September 1993 the Army Surgeon General enlisted the assistance of Dr. Jay Sanford, an expert in infectious diseases and former president of the USUHS, to assess clinical case histories of Gulf War veterans. The goal was to define a standard symptom complex to aid physicians in diagnosis. Dr. Sanford completed his review and submitted his preliminary findings on January 27, 1994. Dr. Sanford concluded that the cases available for review at the time lacked the consistent clinical findings necessary to establish a case definition which meets the criteria of being sensitive enough to identify individuals with a new illness but specific enough to exclude individuals with other known illnesses.<sup>19</sup>

By late 1993 it had become evident to the Department that there was a need to have independent scientific bodies review the development of “unexplained illnesses” among Gulf War veterans. In February 1994 the Department tasked the Defense Science Board (DSB) to examine the possible exposure of personnel to chemical and biological weapons agents and other hazardous material during the Gulf War and its aftermath. The DSB Task Force on Persian Gulf War Health Effect, chaired by Dr. Joshua Lederberg, a Nobel laureate, concluded in its June 1994 report that “there is no persuasive evidence that any of the proposed etiologies caused chronic illness on a significant basis.”<sup>4</sup> The National Institutes of Health (NIH) Technical Assessment Workshop on the Persian Gulf Experience and Health, a panel of non-federal experts formed to assess existing data on the “unexplained illnesses” being reported by Persian Gulf veterans, was convened from April 27-29, 1994, by the DoD, VA, and Department of Health and Human Services (HHS). Among its conclusions, the panel indicated that “the complex biological, chemical, physical, and psychosocial environment of the Persian Gulf theater of operations

appears to have produced complex, adverse health effects ... there is no single disease or syndrome apparent, but rather multiple illnesses with overlapping symptoms and causes.”<sup>20</sup>

In response to the magnitude of veterans’ concerns and the uncertainty surrounding the nature of some of their illnesses, the Assistant Secretary of Defense (Health Affairs) announced a three-point plan, on May 11, 1994.<sup>21</sup> The plan included:

1. The development of an aggressive, comprehensive, clinical diagnostic program to offer intensive examinations to veterans who do not have clearly defined diagnoses,
2. An initial independent review of DoD clinical and research efforts concerning the Persian Gulf War by Dr. Harrison C. Spencer, Dean of The Tulane School of Public Health and Tropical Medicine, New Orleans, Louisiana, and
3. The creation of a forum of national medical and public health experts to review, comment, and advise DoD concerning the results of the clinical evaluation program.

This plan represents the Department’s fundamental approach to meeting the health needs of Gulf War veterans. The CCEP offers in-depth medical examinations through a program which provides prioritized access to clinical care through the Military Health Services System (MHSS). Dr. Spencer of Tulane provided an initial review of the issue of “unexplained illnesses” and recommended development of a standardized clinical protocol even in the absence of a specific case definition. External review of the Department’s clinical program, both design and implementation, has been a key component in the overall approach to providing care to Gulf War veterans. External scientific review has been provided by the Institute of Medicine (IOM), National Academy of Sciences. The IOM Committee on the DoD Persian Gulf Syndrome Comprehensive Clinical Evaluation Program has provided ongoing consultation regarding the CCEP. DoD clinicians have presented the results from the CCEP to the IOM expert committee on three occasions. This collaborative process has proven successful in enhancing the quality of

care provided through the CCEP and in characterizing the clinical nature of illnesses being experienced by CCEP participants.

### **CCEP Specialized Care Center (SCC)**

A Specialized Care Center (SCC) opened at Walter Reed Army Medical Center in March 1995 for the intensive treatment of symptomatic Persian Gulf War veterans. Referrals are accepted from clinicians who have evaluated veterans in the CCEP. Clinicians are requested to refer motivated individuals to the SCC who are suffering from persistent symptoms that interfere with their ability to perform their duty or to meet fitness and retention standards.

Patients come to the SCC for four-week treatment periods in groups of four to six and reside on the grounds of Walter Reed as outpatients. They receive treatment from a multidisciplinary team that includes fitness trainers, nutritionists, occupational and physical therapists, art and recreation therapists, internists, social workers, psychiatrists, and psychologists. The program is rigorous, beginning at 0600 each morning and extending into the evening.

Thirty-five veterans have entered the program, with only one failing to complete the four weeks. Five patients have completed a program specifically tailored to veterans with PTSD. Nearly all patients have shown improvement in their health and a significant improvement in their level of fitness. The latter is demonstrated by an average two-minute decrease in the time required to complete a two-mile run. Although not overwhelmed with patients, the SCC continues to accept referrals as needed. A second SCC is scheduled to open at Wilford Hall Medical Center, Lackland AFB, Texas in mid 1996. Patients who have completed the SCC programs will receive follow-up as clinically indicated.

### **Institute of Medicine Review**

As noted above, the Department of Defense asked the IOM to establish a committee to evaluate the CCEP. The IOM was chartered in 1970 by the National Academy of Sciences to enlist

distinguished members of appropriate professions to examine policy pertaining to the health of the public. The IOM Committee has reviewed the clinical evaluation protocol and commented on the interpretation of the CCEP results. In addition, the Committee has provided recommendations relevant to the conduct of the clinical evaluations in the future. The Committee's recent report, released January 4, 1996, included the following recommendations and comments:<sup>22</sup>

- The CCEP clinical protocol is a thorough, systematic approach to the diagnosis of a wide spectrum of diseases.
- The DoD is encouraged to emphasize in its future reports psychosocial stressors that can produce physical and psychological effects.
- There is currently no clinical evidence in the CCEP for a previously unknown, serious illness among Persian Gulf War (PGW) veterans. Several large research studies currently being conducted by DoD and the VA may provide more definitive answers as to the possibility of a new or unique Persian Gulf syndrome.
- Interpretations based on comparisons with other populations should be made with great caution and only with the explicit recognition of the limitations of the CCEP as a self-selected case series.
- The results of the CCEP can and should be used for several purposes, including education, improving the medical protocol itself, and evaluating patient outcomes.

### **Persian Gulf Veterans' Coordinating Board**

The Persian Gulf Veterans Coordinating Board, consisting of the Secretaries of Defense, Veterans Affairs, and Health and Human Services was established on January 21, 1994 by President Clinton to merge the expertise and capabilities of the departments and coordinate all

efforts on behalf of Persian Gulf veterans. The Coordinating Board is composed of three working groups with representation from each of the agencies that focus on issues of research, clinical care, disability evaluation and compensation.

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## **What's New in This Report**

Since June 1994 over 19,000 Persian Gulf veterans have completed medical evaluations within the DoD CCEP worldwide. This report encompasses the results on 18,598 CCEP participants and is largely consistent with results of previous CCEP reports. For example, the frequency distribution of self-reported exposures, symptoms and diagnoses have remained relatively constant since the CCEP began.

This report reflects recommendations from the IOM and other consultants to DoD. Areas that have been explored in greater detail include analysis of a subpopulation of the National Ambulatory Medical Care Survey (NAMCS), which resembles the CCEP population in terms of sex and age; characterization in greater detail of those individuals with more than one diagnosis; an evaluation of disability associated with CCEP participants; analysis and examination of the reproductive questionnaire that was introduced in January 1995; review of the distribution of diagnostic categories over time intervals; and further analysis of unit identification codes (UICs) as a surrogate measure of occupational exposure and location within the Persian Gulf theater of operation.

# METHODS

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Participants may enroll in the CCEP by calling a toll-free number (1-800-796-9699), which provides information and referrals to individuals requesting medical evaluations or by contacting their local military medical treatment facility (MTF). All MHSS eligible beneficiaries are eligible for the CCEP. For eligibility in the CCEP, a PGW veteran (or dependent) must have been eligible for DoD health care in June 1994 or later.

Once an individual is referred, the CCEP provides a two-phase, comprehensive medical evaluation, with Phase I being conducted at one of 184 local MTFs. Phase II (when required) is conducted at one of 14 regional medical centers (RMCs). The medical review includes questions about family history, health, occupation, and unique exposures in the Gulf War, as well as a structured review of symptoms.

Once a participant has completed the examination process, copies of examination results are forwarded to the CCEP Program Management Team (PMT), where they undergo quality assurance procedures, and the data are entered into the master CCEP database.

Additionally, for those CCEP participants suffering from chronic, debilitating symptoms, the DoD has established an SCC at Walter Reed Army Medical Center and will have a second center opening in mid 1996 at Wilford Hall Medical Center, Lackland AFB, Texas.

The data, which were initially entered into a relational database, were translated into a statistical format for this report. Various validity checks were conducted to ensure that the data were appropriate for interpretation. Statistical tests and descriptive analyses were conducted on various categories of participants, including those in theater during the Persian Gulf War, their spouses, and their children. Moreover, the CCEP participants who were in theater were compared to the PGW population as a whole and were stratified by units to compare those units

with higher CCEP participation to those units with lower CCEP participation. Specific analyses concerning self-reported exposures, physician-elicited symptoms, diagnoses, self-reported reproductive outcomes, self-reported lost workdays, physical evaluation boards (PEBs), and program satisfaction were conducted. Additionally, a comparative analysis with the NAMCS data was conducted using age, sex, race, ethnicity, and diagnostic code variables to more closely match the CCEP population.

See Appendix B for more specific information regarding the methods used in data analyses.

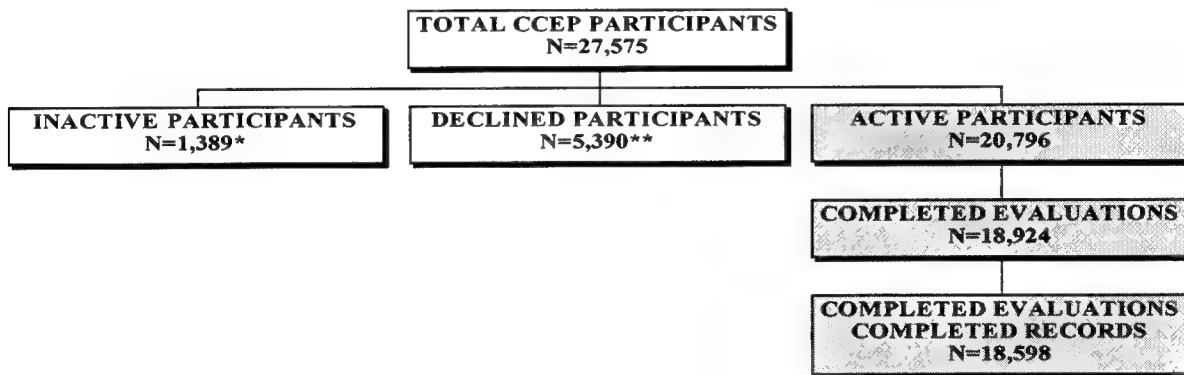
# RESULTS

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## Program Status

Figure 1 summarizes the categories of CCEP participants as of early December 1996. Of the 20,796 participants who requested medical examinations through the CCEP, 18,598 records have been entered into the CCEP computerized database (Figure 1). Eighty-seven percent (87%) of CCEP evaluations were completed at Phase I and 13% at Phase II.

**Figure 1. Disposition of CCEP Participants as of December 6, 1995**



\* Inactive Participants include those participants who wish to defer their medical evaluation until a later time.

\*\* Declined Participants are those participants who have determined that they do not desire to undergo the evaluation process (but do desire to be registered in program) and subsequently signed a declination form OR are those participants who have not responded to the repeated phone calls/certified return receipt letters requesting that they contact their local CCEP Administrator in order to schedule an appointment to begin or continue their examination process.

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## Demographics

Demographic characteristics of the in-theater CCEP participants are shown in Table 1 along with comparable data for the total PGW participants. The total PGW participants are defined as all active duty personnel plus all Reserves/Guard who were actually in the Gulf War theater. The Army is more heavily represented in the CCEP database than other military branches. Also, higher percentages of women and blacks are found in the CCEP database when compared to all PGW participants. The age distribution of CCEP participants differs from the total Gulf War participants in that the CCEP participants have a higher percentage of individuals in the two oldest age groups (44.3%) than the total PGW participants (28%). With the exception of the youngest age group, the CCEP participants are spread approximately uniformly across the remaining four groups.

**Table 1. Demographic Characteristics of CCEP Participants and Persian Gulf War Participants**

Characteristics	CCEP Participants N=18,075 <sup>#</sup>	Total PGW Participants N=697,000*
Gender(%)		
Male	88	93
Female	12	7
Race(%)		
White	57	70
Black	32	23
Hispanic	6	5
Other/No Data	5	2
Age <sup>†</sup>		
Mean	30	26 <sup>‡</sup>
Median	29	24 <sup>‡</sup>
In Groups(%)		
17-20	10	11
21-25	23	38
26-30	23	22
31-35	22	13
36-65	22	15
Other/No Data	1	
Rank(%)		
Enlisted	88	89
Officer	11	10
Other/No Data	1	1
Branch(%)		
Air Force	10	12
Army	81	50
Marines	4	15
Navy	4	23
Other/No Data	1	---
Status(%)		
Active	83	83
Reserve Component <sup>††</sup>	13	17
Other/No Data	4	---

<sup>#</sup> Includes only CCEP members in theater.

\* Source: Desert Shield/Storm Participation Report Vols. 1 & 2. Defense Manpower Data Center, DoD, 1994.

<sup>†</sup> Participant's Age as of 2 August 1990.

<sup>††</sup> Because most RC PGW participants are not military health care beneficiaries, these differences are expected.

<sup>‡</sup> Mean and median age and marital status for PGW veterans are for Active Component members only.

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## Self-Reported Exposures

The self-reported responses to a checklist of 25 exposures are summarized in Table 2. Most participants reported at least one exposure. Only 0.2% of CCEP participants reported no exposure. The median number of self-reported exposures was ten.

The most frequent self-reported environmental exposures include passive cigarette smoke (88%), diesel/other fuels (88%), pyridostigmine bromide tablets (74%), oil smoke (71%), tent/heater fumes (70%), and personal pesticide use (66%). Least often self-reported exposures were suspected nerve gas/nerve agents (6%), suspected mustard/blistering agents (2%) and wounded in combat (2%). Nearly one-third (31%) of the CCEP in-theater participants indicate they are current smokers, smoking an average of 15 cigarettes per day.

Five questions were related to exposures associated with combat. Ten percent of the participants reported none of these, 40% reported one or two, and 21% four or five. The most frequently reported of these exposures were witnessing a chemical alarm, witnessing a casualty, and witnessing SCUD attacks. Only 2% self-reported being wounded in combat.

**Table 2. Self-Reported Exposure History (N=18,075)**

Exposures Recalled By Participants	Response	
	Number	Percent*
Cigarette Smoke (Passive)	15,993	88
Diesel/Other Fuels	15,910	88
Pyridostigmine Bromide	13,287	74
Oil Fire Smoke	12,763	71
Tent/Heater Fumes	12,651	70
Personal Pesticide Use	11,891	66
Ate Non-U.S. Foods	11,848	66
Had Anthrax Immunization	8,881	49
Solvent	8,708	48
Chemical Agent Resistant Coating (CARC) Paint	8,444	47
Other Paint	7,755	43
Microwaves	6,124	34
Bathed in/Drank Non-U.S. Water	5,835	32
Had Botulism Immunization	4,696	26
Took Oral Medicine to Prevent Malaria	3,926	22
Ate Contaminated Food	3,773	21
Bathed in Contaminated Water	3,579	20
Depleted Uranium	2,793	15
Nerve Gas/Nerve Agents	1,056	6
Mustard Gas/Blistering Agents	429	2
Chemical Alarm	11,806	65
Witnessed Casualty	10,124	56
Witnessed SCUD Attack	9,743	54
Witnessed Actual Combat	6,746	37
Wounded in Combat	314	2

\* Percent of participants who answered Yes or No (excludes unknown).

## Physician-Elicited Symptoms

Table 3 summarizes the frequency distribution of positive responses to the Provider-Administered Symptom Questionnaire. The most frequently reported chief complaints were: fatigue (10%), joint pain (11%), headache (7%), and/or memory loss (4%). The percentages of patients reporting any of the major complaints included fatigue (47%), joint pain (49%),

headache (39%), memory loss (34%), sleep disturbance (32%), rash/dermatitis (31%), and/or difficulty concentrating (27%).

**Table 3. Symptom Frequency for CCEP Participants (N=18,075)**

Symptoms Reported By Participants	Chief Complaint (%)	Any Complaint (%)
Joint Pain	11	49
Fatigue	10	47
Headache	7	39
Memory Loss	4	34
Sleep Disturbance	2	32
Rash/Dermatitis	7	31
Difficulty Concentrating	*	27
Depression	1	23
Muscle Pain	1	21
Diarrhea	2	18
Dyspnea	3	18
Abdominal Pain/Gastrointestinal	3	17
Hair Loss	*	12
Bleeding Gums	*	8
Weight Loss	*	7
Allergies	*	*
Back Pain	2	2
Chest Complaints	2	2
Cough	1	1
Dizziness	1	1
Nausea	*	*
Sinus	1	1
Mood Swings	1	1
Insomnia	*	*
Other Chief Complaint Categories Representing <1% of Population	7	7
Chief Complaints Not Categorized	3	3
People with No Chief Complaints	31	
People with No Chief or Any Complaints	10	

\* less than 1%

The distribution of dates of onset of symptoms reported by the CCEP participants is presented in Table 4. Among those reporting a known date of onset, the most common period of onset for all symptoms is the nine-month interval after the Gulf War. Between 23% and 31% of participants who recalled a date of onset for at least one of their symptoms remembered it starting during this period. However, it is noteworthy that for all symptoms, no date of onset was recalled/recorded by over half of all participants. Thus, for over half the symptoms reported, no date of onset can be ascertained. Lacking data collected in closer proximity to the date of onset, the effects of recall bias cannot be discounted, which makes the appropriate interpretation of these data difficult.

**Table 4. Frequency of Date of Onset by Symptom**

Symptoms Reported by Participants	Number Rept. Symptom	Number with Date of Onset	< Aug 1990 %	Aug 90 thru Feb 91 %	Mar 91 thru Dec 91 %	Jan 92 thru Dec 92 %	Jan 93 thru Dec 93 %	Jan 94 thru Dec 94 %	Jan 95 into Dec 95 %
Joint Pain	8,384	3,516	7	15	23	21	15	14	5
Fatigue	8,135	3,283	2	16	31	22	14	11	3
Headache	6,743	2,699	6	18	25	19	14	13	5
Memory Loss	5,960	2,385	2	15	27	23	16	14	3
Sleep Loss	5,887	2,405	4	20	30	19	12	12	3
Rash	5,124	2,230	5	21	29	18	10	11	5
Concentration	4,899	1,834	2	16	30	21	15	13	3
Depression	4,140	1,583	4	18	29	20	13	13	6
Muscle Pain	3,900	1,418	4	17	28	20	13	14	4
Diarrhea	3,304	1,237	4	24	30	16	9	11	6
Shortness of Breath	3,028	1,492	4	14	25	20	15	17	7
Abdominal Pain	3,007	1,167	5	19	24	19	12	14	7
Hair Loss	2,145	872	7	16	29	20	12	12	4
Bleeding Gums	1,500	559	5	16	25	20	15	14	5
Weight Loss	1,235	469	3	19	25	15	11	17	10

## CCEP Diagnoses

Table 5 presents the 23 ICD-9-CM diagnostic codes for primary diagnoses occurring with a frequency of 1% or higher. The healthy diagnosis includes those participants seeking consultation without complaint or sickness as well as those diagnosed as normal or healthy. The specific diagnoses span various categories including psychological conditions; symptoms, signs and ill-defined conditions; and the musculoskeletal, nervous, respiratory, digestive, skin, and circulatory systems. Other than healthy, the frequency of each diagnosis was relatively low, with the highest (tension headache) at 3.4%, and the second highest (fatigue, not specified as chronic) at 3.3%. Appendix C presents additional information on the diagnoses assigned.

**Table 5. Primary Diagnoses Occurring in Greater Than 1% of CCEP Participants (N=18,075)**

Primary Diagnosis ICD-9 CM Code	Number	Percent Of Total
Healthy (V65.5)*	1762	9.7
Tension Headache (307.81)	622	3.4
Fatigue, Not Specified as Chronic (780.71)	595	3.3
Depressive Disorder Not Elsewhere Classified (311.)	525	2.9
Prolonged Posttraumatic Stress Disorder (309.81)	501	2.8
Headache (784.0)	495	2.7
Migraine, Unspecified (346.9)	480	2.7
Pain in Joint Involving Multiple Sites (719.49)	437	2.4
Asthma, Unspecified (493.9)	401	2.2
Lumbago (724.2)	356	2.0
Pain in Joint Involving Lower Leg (719.46)	323	1.8
Other General Symptoms (780.9)	305	1.7
Irritable Colon (564.1)	291	1.6
Allergic Rhinitis, Cause Unspecified (477.9)	286	1.6
Osteoarthritis, Unspecified (715.9)	272	1.5
Malaise and Fatigue (780.7)	267	1.5
Other and Unspecified Sleep Apnea (780.57)	252	1.4
Gastroesophageal Reflux Disease (GERD) (530.81)	251	1.4
Major Depressive Disorder, Single Episode (296.2)	242	1.3
Contact Dermatitis and Other Eczema, Unspecified (692.9)	227	1.3
Other Insomnia (780.52)	210	1.2
Neurotic Depression (300.4)	196	1.1
Essential Hypertension (401.9)	193	1.1

\* This code includes those participants seeking consultation without complaint or sickness as well as those diagnosed as normal and/or healthy.

The frequency distribution by category of diagnoses assigned by the CCEP is presented in Table 6. The most prevalent primary diagnostic categories, accounting for 67.7% of the participants, were psychological conditions (18.4%); musculoskeletal and connective tissue diseases (18.3%); symptoms, signs, and ill-defined conditions (17.9%); respiratory diseases (6.8%); and digestive system diseases (6.3%). An additional 9.7% received a diagnosis of healthy. CCEP clinicians have generally relied upon the common medical practice of determining primary diagnosis based upon the severity of illness relative to the participant's chief complaint.

When both primary and secondary diagnoses were considered, the same general patterns were observed. The most common categories were musculoskeletal diseases (found in 47.2% of participants); symptoms, signs, and ill-defined conditions (43.1%); psychological conditions (36.0%); digestive system diseases (20.4%); skin and subcutaneous diseases (19.9%); respiratory diseases (17.5%); and nervous system diseases (17.8%).

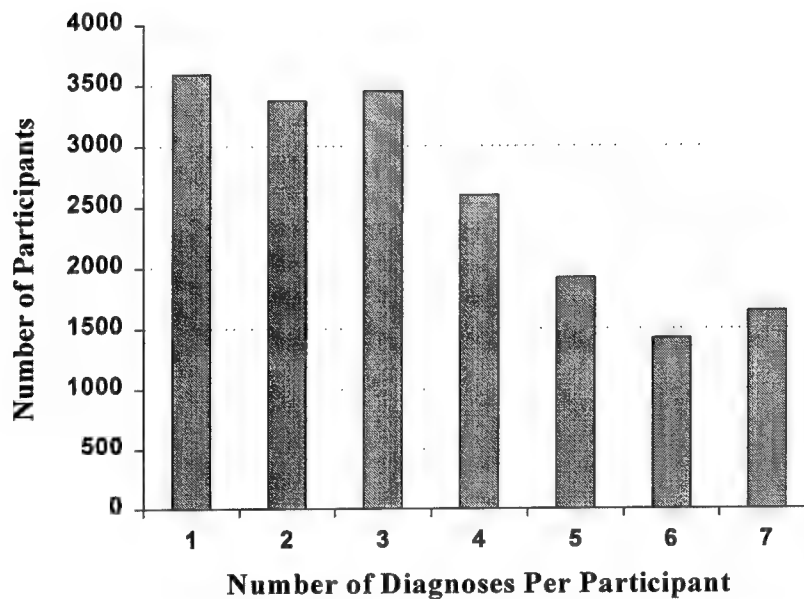
**Table 6. Frequency Distribution of Primary Diagnoses and Any Diagnoses (N=18,075)**

Diagnostic Categories (ICD-9-CM Code)	Male Primary Diagnosis N=15,944 (%)	Female Primary Diagnosis N=2,131 (%)	All Part. Primary Diagnosis N=18,075 (%)	All Part. Any Diagnosis N=18,075 (%)
Psychological Conditions (290-319)	18.3	19.1	18.4	36.0
Symptoms, Signs, and Ill-Defined Conditions* (780-799)	18.1	16.5	17.9	43.1
Musculoskeletal System Diseases (710-739)	18.6	15.9	18.3	47.2
Healthy (V65.5)	9.9	8.6	9.7	10.2
Respiratory System Diseases (460-519)	6.9	6.1	6.8	17.5
Digestive System Diseases (520-579)	6.5	4.9	6.3	20.4
Skin and Subcutaneous Tissue Diseases (680-709)	6.3	6.0	6.2	19.9
Nervous System Diseases (320-389)	5.3	8.8	5.7	17.8
Infectious Diseases (001-139)	2.6	2.5	2.6	9.0
Circulatory System Diseases (390-459)	2.3	1.6	2.2	8.0
Endocrine Disorders (240-279)	1.9	2.7	2.0	7.9
Genitourinary System Diseases (580-679)	1.0	3.6	1.3	5.4
Injury and Poisoning (800-999)	0.8	0.9	0.8	3.2
Neoplasm (140-239)	0.8	0.8	0.8	2.9
Blood and Blood Organ Diseases (280-289)	0.4	1.6	0.5	3.0
Other V Codes	0.2	0.4	0.3	10.3
Congenital Anomalies and Conditions of the Perinatal Period (740-779)	0.2	0.2	0.2	1.1

\* Includes conditions categorized according to ICD-9-CM nomenclature of cases for which no diagnosis is classifiable elsewhere no more specific diagnosis can be made; signs or symptoms that prove to be transient; cases in which a more precise diagnosis was not available for any other reason.

Up to seven diagnoses, including healthy, could be reported (one primary and up to six secondary). Among the participants, 19.9 percent had only 1 diagnosis, 18.7 percent had 2, the median was 3, the mean was 3.4, and 9.1 percent were given 7 diagnoses. This distribution is presented in Figure 2.

**Figure 2. Frequency Distribution of Diagnoses among 18,075 CCEP Participants**



The frequencies of primary diagnoses for four periods since initiation of the CCEP and until December 6, 1995 are presented in Table 7. Over time, there have been some changes in the frequency of diagnosis for most diagnostic categories. The proportion with a primary diagnosis of musculoskeletal/connective tissue disorder has steadily increased, from 16.1% in the first period, to 20% in the last. The proportion with psychological conditions was stable for the first two periods, then declined for the third and was stable through the fourth. The proportion with ill-defined conditions has steadily decreased, from 20.9% in the first period, to 15.2% in the fourth. For other diagnostic groupings, there were no patterns evident over time, or the numbers of diagnoses were too few for meaningful interpretation.

**Table 7. Frequency of Primary Diagnoses Over Time (N=18,075)**

Diagnostic Categories	Jun 94 thru Nov 94 N=3931 (%)	Dec 94 thru Feb 95 N=1782 (%)	Mar 95 thru Jun 95 N=8723 (%)	Jul 95 into Dec 95 N=3639 (%)	Jun 94 into Dec 95 N=18075 (%)
Psychological Conditions	19.9	20.0	17.6	17.6	18.4
Musculoskeletal Diseases	16.1	18.2	18.6	20.0	18.3
Symptoms, Signs, and Ill-Defined Conditions*	20.9	18.3	17.6	15.2	17.9
Healthy (V65.5) <sup>†</sup>	8.0	10.2	10.2	10.5	9.7
Respiratory System Diseases	6.4	5.8	7.3	6.5	6.8
Digestive System Diseases	6.8	6.3	6.0	6.3	6.3
Skin and Subcutaneous Tissue Diseases	4.9	6.0	6.8	6.5	6.2
Nervous System Diseases	6.5	5.0	5.3	6.2	5.7
Infectious Diseases	2.5	2.7	2.5	2.9	2.6
Circulatory System Diseases	2.1	1.8	2.2	2.5	2.2
Endocrine Disorders	2.0	2.1	1.9	2.3	2.0
Genitourinary Diseases	1.3	1.4	1.4	1.1	1.3
Neoplasm	1.0	0.6	0.8	0.7	0.8
Injury and Poisoning	0.5	0.8	0.9	0.9	0.8
Blood and Blood Organ Diseases	0.6	0.5	0.5	0.6	0.5
Other V Codes	0.3	0.2	0.2	0.3	0.2
Congenital Anomalies and Conditions of the Perinatal Period	0.2	0.3	0.2	0.3	0.2

\* Includes conditions categorized according to ICD-9 nomenclature of cases for which no diagnosis is classifiable elsewhere; no more specific diagnosis can be made; signs or symptoms that prove to be transient; and cases in which a more precise diagnosis was not available for any other reason.

<sup>†</sup> This code includes those participants seeking consultation without complaint or sickness as well as those diagnosed as normal and/or healthy.

## Examination of the Top Three Primary Diagnostic Categories

Psychological conditions; symptoms, signs, and other ill-defined conditions; and musculoskeletal diseases diagnostic categories account for over 50% of all primary diagnoses among the 18,075 participants covered by this report. The distribution of these diagnoses is presented in greater detail in Table 8, Table 9, and Table 10.

About eighteen percent (18.4%) of CCEP patients had a primary diagnosis of a psychological condition. The most frequent diagnoses of this group are summarized in Table 8. Tension headache, depression, anxiety disorders, adjustment reactions, and somatoform disorders were the most frequently recorded psychological diagnoses. It is important to realize that the common diagnosis of tension headache is included in this category.

**Table 8. Number and Percent of Primary Diagnoses of Psychological Conditions (ICD-9-CM Codes 290-319) (N=3,321)**

Specific Diagnoses (ICD-9-CM Code)	Number	Percent
Tension Headache (307.81)	622	18.7
Depressive Disorder, NEC (311)	525	15.8
Prolonged Posttraumatic Stress Disorder (309.81)	501	15.1
Major Depressive Disorder (296.2)	289	8.7
Adjustment Reaction (309)	231	7.0
Neurotic Depression (300.4)	196	5.9
Somatization Disorder (300.81)	114	3.4
Anxiety State (300.00)	92	2.8
Alcohol Dependence and Abuse (303 and 305)	52	1.6
Sleep Disorder (307.4)	91	2.7
Unspecified Psychophysiological Malfunction (306.9)	49	1.5
Tobacco Use Disorder (305.1)	44	1.3
Unspecified Acute Reaction to Stress (308.9)	37	1.1
Panic State (300.01)	33	1.0
Organic Brain Syndrome	100	3.0
Generalized Anxiety Disorder (300.02)	26	0.8
Other	319	9.6
<b>Total</b>	<b>3,321</b>	<b>100.0</b>

Almost eighteen percent (17.9%) of participants had a primary diagnosis of symptoms, signs, and ill-defined conditions (Table 9). Most diagnoses in this category involved conditions such as malaise and fatigue, sleep disturbance, and/or headache.

**Table 9. Number and Percent of Primary Diagnoses of Symptoms, Signs, and Ill-Defined Conditions (ICD-9-CM Codes 780-799) (N=3,239)**

Specific Diagnoses (ICD-9-CM Code)	Number	Percent
Malaise and Fatigue (780.7)	862	26.6
Sleep Disturbances (780.5)	574	17.7
Headache (784.0)	495	15.3
Other General Symptoms (780.9)*	305	9.4
Dyspnea and Painful Respirations (786.09, 786.52)	181	5.6
Rash (782.0, 782.1)	159	4.9
Syncope (780.2), Seizures (780.3) & Vertigo (780.4)	94	2.9
Other Chest Pain (786.50, 786.59)	70	2.2
Abdominal Pain (789.0)	43	1.3
Nonspecific Reaction to Tuberculin Test (795.5)	44	1.4
Cough (786.2)	36	1.1
Other	376	11.6
<b>Total</b>	<b>3239</b>	<b>100.0</b>

\* The category "Other General Symptoms" (ICD-9-CM code 780.9) consists almost exclusively of reported problems with memory (137 out of 144).

About eighteen percent (18.3%) of CCEP patients had a primary diagnoses in the category of musculoskeletal and connective tissue conditions (Table 10). Pain in joints, osteoarthritis, and backache accounted for over 50% of all diagnoses in this group.

**Table 10. Number and Percent of Primary Diagnoses of Musculoskeletal Conditions (ICD-9-CM Categories 710-739) (N=3,307)**

<b>Specific Diagnoses (ICD-9-CM Code)</b>	<b>Number</b>	<b>Percent</b>
Pain in Joint (719.4)	992	30.0
Lumbago and Backache, Unspecified (724.2 and 724.5)	411	12.4
Osteoarthritis, Unspecified (715.89 - 715.99)	405	12.2
All Other Diagnoses Related to the Spine (720-724.9 except the above)	269	8.1
Myalgias and Myositis, Unspecified (729.1)	228	6.9
Diseases and Disorders of Shoulder Region (726.10, 726.2)	118	3.6
Other Specified Disorders of Lower Leg Joint (mostly patello-femoral syndrome) (719.86)	109	3.3
Osteoarthritis, Localized (715.1-715.39)	56	1.7
Chondromalacia of Patella (717.7)	37	1.1
Tietze's Disease (733.6)	33	1.0
Unspecified Arthropathy (716)	32	1.0
Other and Unspecified Disorders of Soft Tissue (729.9)	29	0.9
Rheumatoid Arthritis (714)	26	0.8
Lateral Epicondylitis (726.32)	24	0.7
Pain in Limb (729.5)	21	0.6
Flat Foot (734)	19	0.6
Enthesopathy of Hip Region (726.5)	19	0.6
Enthesopathy of Unspecified Site (726.90)	17	0.5
Plantar Fascial Fibromatosis	17	0.5
Other	445	13.5
<b>Total</b>	<b>3307</b>	<b>100.0</b>

The frequency of the most prevalent primary diagnostic categories for the five age groups is shown in Table 11. The frequency of psychological conditions shows some decrease with increasing age. This trend is also seen for the healthy ICD-9-CM diagnosis. The musculoskeletal conditions ICD-9-CM category seems to show increases with increasing age. The four most frequent diagnoses represent from 63% to 65% of the diagnoses in each age group.

**Table 11. Frequency of Most Prevalent Primary Diagnoses by Age Group (N=18,075)**

Diagnostic Category	17 - 20 N=1,717 (%)	21 - 25 N=4,141 (%)	26 - 30 N=4,141 (%)	31 - 35 N=4,031 (%)	36 - 65 N=3,938 (%)	Other*/ No Data N=114 (%)
Psychological Conditions	21	20	18	18	17	25
Symptoms, Signs and Ill-Defined Conditions	16	18	18	18	19	16
Musculoskeletal System Diseases	15	16	18	20	20	18
Healthy	13	11	11	9	7	7
Other Medical Conditions	35	35	35	35	37	34

\* Includes ages under 17 and over 65.

Table 12 shows that the four most frequent primary diagnostic categories represent 65.1% of males and 60.5% of females. The distribution of diagnosis is similar in men and women.

**Table 12. Frequency of Most Prevalent Primary Diagnoses by Sex (N=18,067\*)**

Diagnostic Category	Male N=15,937 (%)	Female N=2,130 (%)
Psychological Conditions	18.3	19.1
Symptoms, Signs and Ill-Defined Conditions	18.1	16.6
Musculoskeletal System Diseases	18.6	15.9
Healthy	10.1	8.9
Other Medical Conditions	34.9	39.5

\* No data is available for 8 participants.

Table 13 shows the frequency of the most prevalent primary diagnostic categories for each military branch. The four most prevalent primary diagnostic categories represent 66.1% of CCEP participants from the Army, 59.5% of Navy participants, 57.7% of Air Force and 58.1% of Marines. Distribution of diagnoses are similar among the services.

**Table 13. Frequency of Most Prevalent Primary Diagnoses by Military Branch (N=18,075)**

Diagnostic Category	Army N=14,588 (%)	Navy N=750 (%)	Air Force N=1,714 (%)	Marine Corps N=781 (%)	Other/ No Data N=242 (%)
Psychological Conditions	18.9	18.0	15.1	16.1	16.1
Symptoms, Sign & Ill-Defined Conditions	17.7	19.3	19.9	17.4	14.5
Musculoskeletal System Diseases	19.0	13.9	15.0	16.5	16.5
Healthy	10.4	8.3	7.6	8.1	11.6
Other Medical Conditions	33.9	40.5	42.3	41.9	41.3

Neoplasms were a primary diagnosis in almost 1% of the participants. A primary diagnosis of malignant disease (Table 14) was found in 52 (0.3 %) of in-theater CCEP participants. The most frequently diagnosed malignant neoplasms were skin cancers and lymphomas.

**Table 14. 52 Cases of Malignant Neoplasms by Sex in CCEP Participants (N=18,075)**

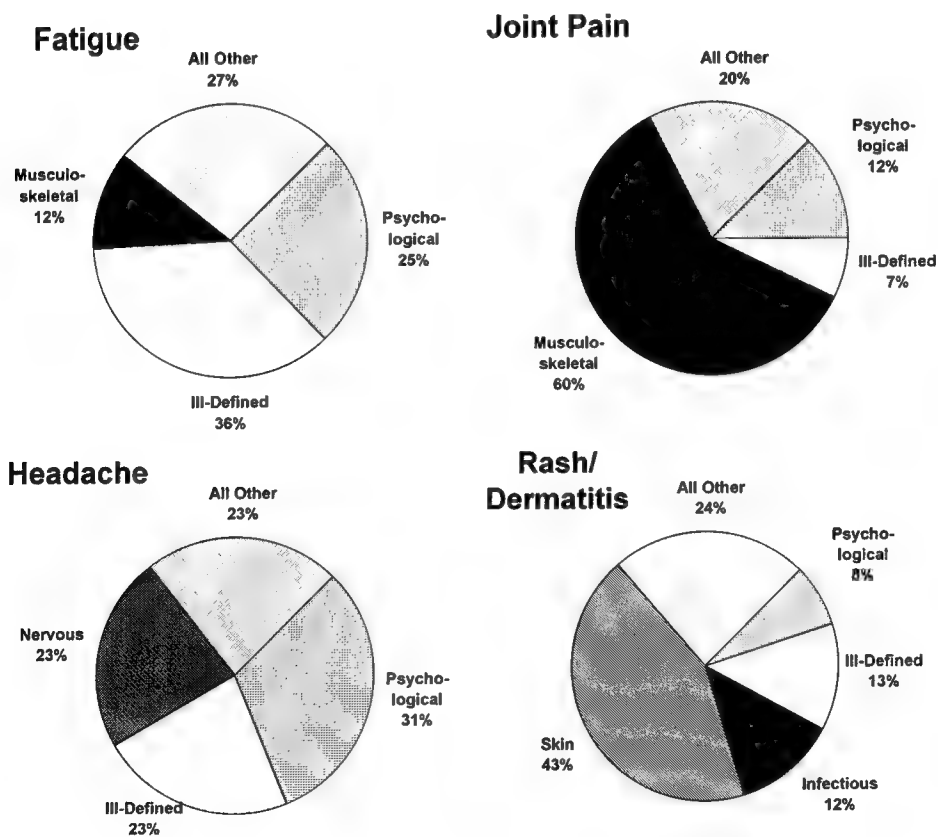
Category	Number Of Diagnoses	
	Male	Female
Skin	9	---
Basal Cell	5	---
Malignant Melanoma	3	---
Squamous Cell	1	---
Hodgkin's Disease	8	---
Non-Hodgkin's Lymphoma	4	1
Brain	5	---
Thyroid	1	1
Prostate	1	---
Testicular and Other Male Gonadal	4	---
Chronic Myelogenous Leukemia	4	---
Chronic Lymphocytic Leukemia	2	---
Acute Myelogenous Leukemia	---	1
Colon	1	---
Breast	---	2
Cervix Uteri	---	1
Ovary	---	1
Stomach	---	1
Lung	3	---
Bladder	1	---
Kidney	1	---
<b>Total</b>	<b>44</b>	<b>8</b>

### **Distribution of Primary Diagnosis Based upon Chief Complaint**

The primary diagnoses associated with the leading chief complaints were examined, and they are presented in Figure 3. Among those participants with a chief complaint of fatigue, the most common diagnostic group was symptoms, signs, and ill-defined conditions; followed by psychological conditions; and musculoskeletal system and connective tissue diseases. Within the diagnostic group of symptoms, signs, and ill-defined conditions, 49% had a primary ICD-9 diagnosis of malaise and fatigue (780.7).

Nearly two-thirds of participants with a chief complaint of joint pain received a primary diagnosis in the musculoskeletal system and connective tissue disease category; followed by symptoms, signs, and ill-defined conditions; and psychological conditions. All other diagnoses accounted for 20% of the total. Among those with a primary diagnosis in the “musculoskeletal system and connective tissue disease” category, 20% had a diagnosis involving multiple sites, and another 20% had a diagnosis involving unspecified sites. There was no apparent clustering of diagnosis by anatomic site.

**Figure 3. Distribution of Primary Diagnoses Based upon Chief Complaint**



The most common category for those with a chief complaint of headache was psychological conditions (31%), followed by symptoms, signs, and ill-defined conditions (23%), and nervous system and sense organs diseases (23%). Among those with a diagnosis within the category of

psychological conditions diagnosis, 67% had a specific diagnosis of tension headache (307.81); among those with a diagnosis within the category symptoms, signs, and ill-defined conditions, 73% had a diagnosis of headache (784.0); and among those with a diagnosis in the nervous system and sense organs category, 77% had a diagnosis of migraine headache (346.0 to 346.9). Thus, among those with a chief complaint of headache, 55% were assigned a primary diagnosis of headache.

Over 40% of CCEP participants with a chief complaint of rash/dermatitis received a diagnosis in the skin and subcutaneous tissue group, followed by symptoms, signs, and ill-defined conditions (13% ), followed by infectious and parasitic diseases (12%), psychological conditions (8%), and all other diagnostic groups (24%). Within the skin and subcutaneous tissue group, 27% had a diagnosis of unspecified contact dermatitis; within the symptoms, signs, and ill-defined conditions 50% had a diagnosis of rash.

## Frequency of Secondary Diagnoses Given a Primary Diagnosis

Table 15 provides the secondary diagnostic groups for participants with a primary diagnosis of psychological condition. The most common second diagnosis for these is also psychological, followed by musculoskeletal. For subsequent diagnoses, psychological, musculoskeletal, and ill-defined conditions predominate. Among those with a primary diagnosis of ill-defined conditions, the most common secondary diagnoses are ill-defined, musculoskeletal, and psychological conditions (Table 16). For those with a primary diagnosis of musculoskeletal, the most prevalent second diagnosis is musculoskeletal, followed by ill-defined conditions, and psychological (Table 17). Those with a primary diagnosis of respiratory were most likely to have a second diagnosis also of respiratory, followed by musculoskeletal, and, symptoms, signs and ill-defined (Table 18).

The patterns of secondary diagnoses change only slightly from diagnosis two through diagnosis seven. This is true for all secondary diagnoses regardless of the primary diagnostic category.

**Table 15. The Proportion of Secondary Diagnoses Given a Primary Diagnosis of Psychological (N=3,321)**

Secondary Diagnosis	Infectious Disease	Neoplasm	Endocrine System	Blood & Blood Disorders	Psychological	Nervous System	Circulatory System	Respiratory System	Digestive System	Genitourinary	Skin & Subcutaneous	Musculoskeletal	Congenital	Ill-Defined	Injury & Poisoning	Healthy
First (%)	2	0	2	1	28	6	2	4	8	1	5	18	0	15	1	7
Second (%)	4	1	3	1	15	7	2	6	9	2	7	22	0	15	1	5
Third (%)	4	1	6	1	10	6	4	9	6	2	8	22	0	16	2	4
Fourth (%)	4	1	2	1	9	7	3	7	9	2	8	22	1	17	2	6
Fifth (%)	3	1	4	1	10	7	4	6	10	2	8	20	1	17	1	5
Sixth (%)	5	1	3	0	11	9	4	6	11	4	7	19	0	15	1	5

**Table 16. The Proportion of Secondary Diagnoses Given a Primary Diagnosis of Symptoms, Signs, and Ill-Defined Conditions (N=3,239)**

Secondary Diagnosis	Infectious Disease	Neoplasm	Endocrine System	Blood & Blood Disorders	Psychological	Nervous System	Circulatory System	Respiratory System	Digestive System	Genitourinary	Skin & Subcutaneous	Musculoskeletal	Congenital	Ill-Defined	Injury & Poisoning	Healthy
First (%)	2	1	2	1	13	5	2	6	8	2	5	21	0	27	1	5
Second (%)	2	1	2	1	11	4	2	6	7	2	7	22	0	27	1	4
Third (%)	2	1	3	1	10	6	2	6	8	2	8	20	1	25	1	5
Fourth (%)	3	1	4	2	12	6	3	6	10	2	7	17	0	24	1	4
Fifth (%)	3	1	4	1	10	7	4	6	9	2	6	18	0	23	2	3
Sixth (%)	3	1	4	1	12	6	4	7	7	3	8	14	1	23	2	5

**Table 17. The Proportion of Secondary Diagnoses Given a Primary Diagnosis of Musculoskeletal (N=3,307)**

Secondary Diagnosis	Infectious Disease	Neoplasm	Endocrine System	Blood & Blood Disorders	Psychological	Nervous System	Circulatory System	Respiratory System	Digestive System	Genitourinary	Skin & Subcutaneous	Musculoskeletal	Congenital	Ill-Defined	Injury & Poisoning	Healthy
First (%)	3	1	2	1	12	6	2	5	5	1	6	27	0	20	2	7
Second (%)	3	1	2	1	14	6	2	5	7	2	8	19	0	24	1	4
Third (%)	3	1	3	0	15	8	3	6	9	2	8	13	1	24	1	4
Fourth (%)	4	1	3	1	13	9	3	6	9	2	7	15	0	22	1	5
Fifth (%)	4	1	4	1	14	7	4	7	11	2	6	12	1	21	1	5
Sixth (%)	4	2	5	2	13	7	6	5	8	2	5	13	0	23	1	6

**Table 18. The Proportion of Secondary Diagnoses Given a Primary Diagnosis of Respiratory (N=1,229)**

Secondary Diagnosis	Infectious Disease	Neoplasm	Endocrine System	Blood & Blood Disorders	Psychological	Nervous System	Circulatory System	Respiratory System	Digestive System	Genitourinary	Skin & Subcutaneous	Musculoskeletal	Congenital	Ill-Defined	Injury & Poisoning	Healthy
First (%)	3	1	2	1	10	6	3	19	6	2	7	17	0	16	1	6
Second (%)	3	1	3	1	14	7	3	8	7	1	8	21	1	18	1	6
Third (%)	4	1	6	1	10	6	4	9	6	2	8	22	0	16	2	4
Fourth (%)	4	1	5	1	10	7	2	9	6	3	10	17	1	18	2	5
Fifth (%)	3	2	3	1	13	6	5	7	9	2	14	14	0	15	1	6
Sixth (%)	3	1	0	1	12	6	3	5	11	5	5	20	1	21	0	8

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## Unit Identification Codes (UICs)

The 687,851 personnel who deployed to the Persian Gulf War, for whom unit identification data are available, were assigned to military units designated by 13,450 unique UICs. The number of deployed personnel assigned to a single UIC varied from one person to several thousand (e.g., an aircraft carrier crew). Additionally, the Air Force used a limited number of large “administrative” UICs (for example one UIC had 20,978 personnel assigned). Of the 18,075 in-theater CCEP participants with completed evaluations, 16,917 had UIC information available. These CCEP participants were assigned to 4,056 different UICs, to which 537,637 service members (77% of the total force) were assigned. The overall rate of CCEP participation for these 4,056 UICs was 3.1% (16,917/537,637). There were no CCEP participants with completed evaluations from at least 9,394 UICs representing about 150,214 service members.

The number of CCEP participants per UIC was examined. The descriptive characteristics of the units are presented in Table 19. After excluding UICs with fewer than 40 members in the Gulf theater and UICs with 1,000 or more members from the analysis, the distribution of CCEP participant rates was stratified into quintiles. Because the quintile of units with highest participation had substantially more members in the CCEP (n=5074) than the lowest quintile (n=1043), the second lowest quintile (n=1331) was combined with the first. Thus, the comparisons are between the CCEP members in the highest quintile to the combined populations of the two lowest CCEP participation rate quintiles.

**Table 19. Descriptive Characteristics of Units in the Lowest and Highest CCEP Participation Groups**

Descriptor	Levels of CCEP Participation	
	Lowest 40%	Highest 20%
Number of UICs	1032	517
Population		
Total Number of Individuals	2374	5074
Unit Size		
Minimum	40	40
Maximum	993	466
Median	139.5	107
Mean	206.4	118
CCEP Participants per Unit		
Minimum	1	3
Maximum	15	37
Median	2	9
Mean	2.3	9.8
Percentage of Unit Members Who Are CCEP Participants		
Minimum	0.12	6.3
Maximum	2.7	26.2
Median	1.4	7.8
Mean	1.4	8.6

The self-reported exposures for the groups are presented in Table 20, along with those for all CCEP members. Based on data from participants who responded with either a yes or no, there are few differences among those in the highest and lowest participation groups.

**Table 20. Self-Reported Exposure History for Members of Units with Lowest and Highest CCEP Participation Rates\***

Exposure As Recalled By Participants	Lowest 40% N=2374	Highest 20% N=5074	CCEP Pop. N=18,075
Cigarette Smoke (Passive)	92	91	90.9
Diesel/Other Fuels	92	95	93.4
Pyridostigmine Bromide	85	92	85.7
Oil Fire Smoke	84	85	81.0
Tent/Heater Fumes	61	83	74.0
Personal Pesticide Use	74	75	74.1
Ate Non-U.S. Foods	70	67	69.4
Had Anthrax Immunization	81	85	81.6
Solvent	76	76	75.9
Chemical Agent Resistant Coating (CARC)	67	74	69.8
Other Paint	73	71	71.0
Microwaves	51	45	48.8
Bathed in/Drank Non-U.S. Water	42	31	36.7
Had Botulism Immunization	60	67	61.8
Took Oral Medicine to Prevent Malaria	66	78	70.3
Ate Contaminated Food	52	50	46.8
Bathed in Contaminated Water	46	44	41.3
Depleted Uranium	32	37	35.3
Nerve Gas/Nerve Agents	23	20	19.7
Mustard Gas/Blistering Agents	8	6	5.6
Chemical Alarm	70	66	65.3
Witnessed Casualty	58	62	56.0
SCUD Attack	51	57	53.9
Witnessed Actual Combat	41	42	37.3
Wounded in Combat	2	2	1.7

\* Exposures expressed as percent of participants who answered Yes or No (excludes unknowns).

The symptoms reported by the participants answering yes or no is given in Table 21. There are few differences between the populations in the higher and lower quintile UICs.

**Table 21. Symptom Frequency for Members of Units with Lowest and Highest CCEP Participation Rates**

Symptom As Elicited By Physician	Lowest 40% N=2374 (%)	Highest 20% N=5074 (%)
Fatigue	46	42
Abdominal Pain	17	15
Diarrhea	19	17
Shortness of Breath	18	16
Difficulty Concentrating	27	25
Hair Loss	11	12
Headaches	37	36
Joint Pain	44	46
Memory Loss	34	31
Muscle Pain	21	20
Rash	28	26
Sleep Disturbance	33	31
Weight Loss	8	6
Bleeding Gums	8	8
Depression	23	22

Table 22 presents the primary diagnoses given to the participants. There were no major differences in the distribution of diagnoses between the two participant categories.

**Table 22. Frequency Distribution Comparison of Primary Diagnoses for Members of Units with Lowest and Highest CCEP Participation Rates**

<b>Primary Diagnostic Categories (ICD-9-CM Code)</b>	<b>Lowest 40% N=2374 (%)</b>	<b>Highest 20% N=5074 (%)</b>
Psychological Conditions (290-319)	19	19
Musculoskeletal Diseases (710-739)	16	19
Symptoms, Signs and Ill-Defined (780-799)	18	18
Healthy (V65.5)	8	11
Digestive System (520-579)	7	6
Respiratory System (460-519)	7	7
Skin and Subcutaneous (680-709)	6	6
Nervous System and Sensory (320-389)	7	5
Infectious Diseases (001-0139)	3	2
Circulatory System (390-459)	2	2
Endocrine/Nutritional (240-279)	2	2
Genitourinary System (580-679)	1	1
Neoplasms (140-239)	1	1
Injury and Poisoning (800-999)	1	1
Blood and Blood-Forming (280-289)	0	1
Congenital Anomalies (740-779)	0	0

The proportion of all diagnoses given is shown in Table 23. There were few substantial differences in the diagnostic categories reported between high and low participation UICs.

**Table 23. Frequency Distribution of Any Diagnoses for Members of Units with Lowest and Highest CCEP Participation Rates**

Any Diagnosis	Lowest 40% N=2374 (%)	Highest 20% N=5074 (%)
Psychological Conditions	37	36
Musculoskeletal System Diseases	44	49
Symptoms, Signs and Ill-Defined Conditions	41	43
Respiratory System Diseases	18	17
Digestive System Diseases	23	19
Skin and Subcutaneous Tissue Diseases	19	20
Nervous System Diseases	20	17
Infectious Diseases	9	8
Circulation System Diseases	8	8
Endocrine Disorders	9	7
Genitourinary System Diseases	6	5
Neoplasms	3	3
Injury and Poisoning	3	4
Blood and Blood Organ Diseases	9	7
Congenital Disorders	1	1

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## Disability Indicators

### Self-Reported Lost Workdays

As an approximation of the severity of morbidity or acute disability, CCEP participants were asked the question, "How many workdays were lost due to illness (last 90 days)?" Approximately 20% of all participants reported missing any workdays. The extent to which the CCEP disability experience reflects the overall disability of Persian Gulf veterans is limited by the fact that many Persian Gulf War veterans are no longer on active duty.

Table 24 shows that the percent of participants reporting “1-90” did not differ greatly between ICD-9-CM categories (range: 10% - 26%). Among the ICD-9-CM code groups, the mean number of workdays lost ranged from one to nine. Neoplasms represent the disease category with the greatest mean number of missed workdays at 9 for the 20 percent reporting any lost workdays. For those reporting lost workdays, the median number of workdays lost ranged from four to six for most diagnoses, with the exception of neoplasms, having a median of 15, and respiratory conditions, having a median of 8.5.

**Table 24. Workdays Lost to Illness in Past 90 Days by Primary Diagnosis (N=18,075)**

Primary Diagnosis	Number of Participants	Total Days Lost	Mean Days Lost	Participants Reporting 1-90 Days Lost		
				%	Mean	Median
Infectious Diseases	470	1,120	2.4	19.2	12.4	6.0
Neoplasms	144	1,301	9.0	16.4	34.2	15.0
Endocrine Disorders	461	1,045	2.3	22.1	10.2	5.0
Psychological Conditions	3,321	12,211	3.7	24.6	14.9	6.0
Nervous System Diseases	1,029	3,533	3.4	26.0	13.2	5.0
Circulatory System Diseases	396	956	2.4	20.7	11.7	5.0
Respiratory System Diseases	1,229	2,733	2.2	22.4	9.9	8.5
Digestive System Diseases	1,131	2,822	2.5	25.6	9.7	4.0
Genitourinary System Diseases	236	632	2.7	25.8	10.4	5.0
Skin and Subcutaneous Tissue Diseases	1,125	1,559	1.4	16.0	8.7	4.0
Musculoskeletal System Diseases	3,307	6,757	2.0	18.1	11.3	5.0
Congenital Anomalies and Perinatal Conditions*	41	53	1.3	14.6	8.8	5.0
Symptoms, Signs and Other Ill-Defined Conditions	3,239	7,169	2.2	19.0	11.6	5.0
Injury and Poisoning	141	435	3.1	21.3	14.5	6.0
E and V Codes (“Healthy”)	1,805	1,445	0.8	10.2	9.8	4.0
<b>Total</b>	<b>18,075</b>	<b>43,771</b>	<b>2.4</b>	<b>20.1</b>	<b>12.0</b>	<b>5.0</b>

\* Includes one case of angiomas of undetermined etiology (25 days), one case of bicuspid aortic valve insufficiency (2 days), one case of dysplastic hip disease (10 days), one case of congenital bilateral hip dysplasia (10 days), one case of spondylolisthesis (1 day) and one case of polycystic kidney disorder (5 days).

## DoD's Physical Evaluation Board Experience

Physical Evaluation Boards (PEBs) are medical boards convened to evaluate whether or not a service member's diagnosed condition precludes their retention in the Armed Services. The findings of PEBs were reviewed as another indicator of severity of morbidity and disability. Comparisons of the PEB results for DoD CCEP participants and PGW veterans who are not CCEP participants are shown in Table 25. Of those CCEP participants who met PEBs 56% received medical separations. Seventy-seven percent of the non-CCEP PGW veterans who were referred to PEBs were medically separated.

**Table 25. Comparison of PEB Experience for Non-CCEP PGW Veterans and CCEP Participants**

	CCEP In-Theater Participants	Non-CCEP PGW Veterans
Population	N=17,833*	N=678,864*
Met PEB (%)	988 (5.5%)	13,117 (1.9%)
Medical Separation	549 (3.1%)	9,550 (1.4%)

\* Population excludes Coast Guard in PGW.

There are 93,944 service members who have undergone PEBs since August 1, 1990, of whom 14,105 were Gulf War veterans. These data reflect only the DoD's disability experience and do not contain the results of non-DoD disability proceedings. Of those service members meeting PEBs since August 1990, 14.3 percent were PGW veterans. Eight percent of PGW veterans meeting PEBs were CCEP participants.

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## Diagnoses Among Family Members

### Diagnoses Among Spouses

The frequency of primary and any diagnoses for spouses of PGW veterans is provided in Table 26. The distribution of diagnoses of military participants compared to spouses is very similar.

**Table 26. Distribution of Primary Diagnoses and Any Diagnosis for Spouses (N=332)**

Diagnostic Categories	Spouses	
	Primary Diagnosis (%)	All Diagnoses (%)
Psychological Conditions	20.8	39.5
Musculoskeletal System Diseases	9.9	33.7
Symptoms, Signs and Ill-Defined Conditions	14.5	42.2
Healthy	9.9	5.4*
Respiratory System Diseases	4.2	15.7
Digestive System Diseases	4.8	23.5
Skin and Subcutaneous Tissue Diseases	7.8	22.6
Nervous System Diseases	8.7	18.1
Infectious Diseases	1.5	7.2
Circulatory System Diseases	1.8	7.2
Endocrine Disorders	5.1	12.3
Genitourinary System Diseases	8.4	17.8
Neoplasms	0.6	3.6
Injury and Poisoning	0.3	2.4
Blood and Blood Organ Diseases	0.9	4.5
Congenital Abnormalities and Conditions of the Prenatal Period	0.3	1.5

\* Includes spouses having a healthy primary and no secondary diagnoses.

## Diagnoses Among Children

Table 27 presents the number of children who are CCEP participants within each primary diagnostic category. The most common diagnosis is healthy, followed by congenital abnormalities, skin conditions, other, and respiratory conditions.

**Table 27. Frequency Distribution of Primary Diagnosis for CCEP Children of Persian Gulf War Veterans (N=191)**

Diagnosis	Number
Healthy (Normal Exam)	72
Congenital Anomalies*	35
Dermatitis, Eczema, Folliculitis, Acne	14
Other	11
Upper Respiratory Infections	9
Asthma, Reactive Airway Disease	6
Psychosis, Depression, Obsessive/Compulsive Disorder	6
Otitis Media	6
Attention Deficit/Hyperactivity	5
Seizures	5
Developmental Delay	4
Gastroesophageal Reflux	4
Nephritis, Vesicoureteral Reflux, Hydrocele	4
Dermoid Cysts, Hemangiomas	3
Rash	2
Anemia	1
Choroid Plexus Carcinoma	1
Chronic Pneumonia	1
Insomnia	1
Tinea Capitis	1
<b>Total</b>	<b>191</b>

\* Specific diagnoses include: congenital heart disease (3); cleft lip or palate (5); chromosomal abnormalities (4); hydrocephalus (5); minor congenital defects (11), including duplicated toe and pectus excavatum; and others (7).

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## Self-Reported Reproductive Events and Conditions

Table 28 displays the proportion of participants self-reporting reproductive events and conditions in the periods three years prior to and three years after ODS/S. There were 8,819 participants who provided information on both the pre- and postwar periods. With the exception of conceptions, which decreased 5%, there were increases in the frequencies of all other reproductive events and conditions. The self-selection of participants into the CCEP and their self-reporting of reproductive events and conditions makes interpretation of these data problematic. This issue is described further in the Discussion section.

**Table 28. Frequency of Self-Reported Reproductive-Events and Conditions (N=8,819)**

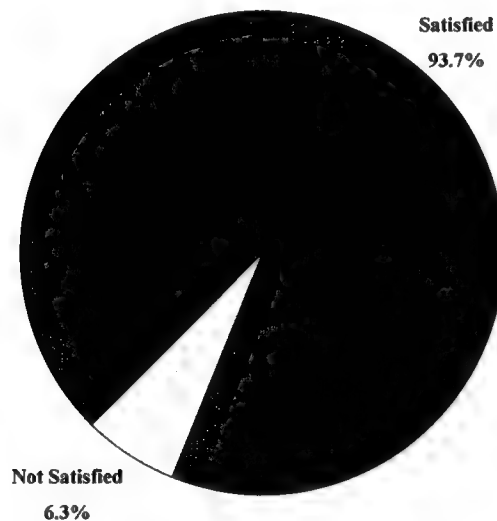
Frequency Of Self-Reported Events And Conditions		
Event/Condition	Proportion Reporting Events	
	3 Years Prior	3 Years Post
Any Children Conceived	31.4	29.9
Infertility	6.2	13.7
Any Miscarriages	5.3	7.8
Any Stillbirths	0.8	1.0
Any Infant Deaths	0.3	0.5
Any Children with Birth Defects	0.7	2.6

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## Participants' Satisfaction

Beginning in January 1995, CCEP participants were asked at the completion of their examination to indicate their opinion of the care they received by answering the question "Were you satisfied with the care you received in the program?" Responses were available for 68% of in-theater participants. Figure 4 shows an overall satisfaction rate of 93.7% for the 12,283 CCEP participants who answered the question regarding satisfaction.

**Figure 4. Participants' Satisfaction (N=12,283)**



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## Comparison of Diagnoses in CCEP to NAMCS

The distributions of primary diagnostic categories for CCEP participants and for subjects from the National Ambulatory Medical Care Survey (NAMCS) are presented in Table 29 for persons aged 20-40 years. Because there are basic underlying differences between the CCEP and the NAMCS populations, caution must be exercised in interpreting the data. CCEP participants generally have health complaints or health concerns sufficient to cause them to seek evaluation. Data on persons in the NAMCS population represent individuals seeking medical attention for unknown reasons, which could include concerns over specific conditions as well as routine examinations in the absence of any adverse condition.

Compared to the NAMCS population, men in the CCEP population were two to five times more likely to receive a diagnosis in the categories of psychological conditions; signs, symptoms, and ill-defined conditions; and musculoskeletal conditions. The proportion with a diagnosis of healthy did not differ substantially, and CCEP participants were less likely to receive a diagnosis in the respiratory, nervous, infectious disease, and skin categories. For the other categories, there were few differences between the CCEP and NAMCS populations, or the proportions in the categories were too low for meaningful interpretation.

Among women, CCEP participants were much more likely to receive a diagnosis in the categories of psychological conditions; signs, symptoms, and ill-defined conditions; and musculoskeletal conditions (by a factor of three or more). CCEP women were much less likely to receive a diagnoses of healthy (8.8% compared to 27%) or a diagnosis in the genitourinary group (3.6% compared to 10.0%). As with the men, it is difficult to assess the other diagnostic categories.

**Table 29. Frequency of Primary Diagnoses for CCEP and NAMCS, by Sex, for Subjects Aged 20-40 Years**

Primary Diagnosis	MEN Age 20-40 Percent Primary Diagnosis		WOMEN Age 20-40 Percent Primary Diagnosis	
	CCEP	NAMCS	CCEP	NAMCS
Psychological Conditions	18.0	7.1	18.0	5.6
Symptoms, Signs and Ill-Defined Conditions	18.0	3.5	17.0	3.2
Musculoskeletal System Diseases	19.0	9.1	16.0	5.3
Healthy	10.0	11.0	8.8	27.0
Respiratory System Diseases	6.7	11.0	6.1	10.0
Skin and Subcutaneous Tissue Diseases	6.3	8.7	6.3	7.2
Digestive System Diseases	6.4	5.2	4.8	3.0
Nervous System Diseases	5.4	9.2	9.0	7.4
Infectious Diseases	2.7	5.5	2.6	3.9
Circulatory System Diseases	2.1	3.2	1.6	2.0
Endocrine Disorders	1.8	2.1	2.6	2.8
Genitourinary System Diseases	0.9	4.6	3.6	10.0
Neoplasms	0.7	2.1	0.8	2.6
Injury and Poisoning	0.8	17.0	1.0	6.6
Blood and Blood Organ Diseases	0.4	0.2	1.7	0.3
Other	0.2	0.3	0.2	2.6

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# DISCUSSION

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## Limitations in Interpreting Results of the CCEP

The CCEP represents an effort by DoD to complete a very large series of comprehensive medical examinations on Persian Gulf War veterans who request evaluation. As a result of proactive case finding and outreach efforts, DoD has conducted systematic medical evaluations on over 18,500 patients. This number includes approximately 3,000 patients who were referred to specialists for more extensive, sophisticated diagnostic workups at one of 14 tertiary care medical centers within the Military Health Services System.

The results of the CCEP characterize the nature of symptoms and the types of diagnoses in this select group of veterans and provide substantial clinical information to describe their general health. However, multiple methodological limitations associated with the CCEP need to be understood to interpret findings appropriately in this population:

- The CCEP population is not a homogeneous group, since it is composed of individuals with health complaints they believe may be related to their service in the Gulf War; others have no current problems but are concerned about their future health status, and a small number of CCEP participants have no current health problems or concerns but simply want to become part of the CCEP registry.
- Since the CCEP represents individuals who have self-selected to enter the program and excludes individuals who are not eligible for care through the military medical system, the CCEP population may not be representative of the overall population of PGW veterans. It is also likely that any Gulf War veterans who are very disabled by illness would no longer be on active duty.

- Throughout this report, findings of available studies on other populations are provided. None of these study populations are fully comparable to PGW veterans and thus any comparisons must be made with caution.
- A case series, such as the CCEP, is not definitive in determining causality or in specifically defining associations between health outcomes and specific risk factors.
- Lack of a case definition or other specific clinical criteria for participation in the CCEP limits the usefulness of inferences that may be drawn in attempting to discern a defined clinical syndrome.

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## Demographics

In terms of demographic characteristics, such as branch of service, sex, age and race, CCEP participants are a broad cross section of service members who deployed to Operations Desert Shield/Storm.

When the demographic characteristics of CCEP participants are compared against all those who deployed to the Persian Gulf, given the large sample sizes, a statistically significant difference was noted for each of the demographic variables (gender, race, age, marital status, rank, branch of service, status), with the exception of enlisted rank. Of interest are the observations that Army personnel, women, individuals over the age of 25, and Blacks appear overrepresented, while Navy personnel, Marines, and Whites appear underrepresented in the CCEP when compared to all other Persian Gulf War veterans.

Given the self-selected, non-random nature of participants in the CCEP, it is difficult to draw any meaningful conclusions from these demographic differences, other than to say that CCEP participants are a self-selected non-random sample of the Persian Gulf War veteran population. Only well-designed epidemiologic studies that compare the CCEP subpopulation with an appropriately matched comparison population will provide the best information on which to base

further investigations regarding any demographic differences. DoD, VA, and HHS have undertaken a number of epidemiologic studies to understand better the health consequences of service in the Gulf War. Appendix A lists the current DoD research projects.

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## **CCEP Participation Rates and Unit Identification Codes (UICs)**

The data comparing the exposures, symptoms, and diagnoses of members of units in the two lowest quintiles of CCEP participation with those of members of units in the highest quintile of CCEP participation provide little evidence of meaningful differences in self-reported exposures, symptoms, or diagnoses between the two groups. While members of the highest participation units reported more frequent exposures to tent heater fumes and antimalarial drugs, the meaning of this is not known. Both of these exposures were very widespread among CCEP participants in general, and these members did not report more symptoms or have more diagnoses.

UICs are in a sense rough surrogates for occupational, temporal, and/or geographic information. Analysis of CCEP results by unit of assignment is potentially an important area for further evaluation. As detailed geographic and temporal information becomes available in 1996, it will be possible to compare UICs in the CCEP population with a variety of epidemiologic and location variables. Examination of unit location by date with an integrated geographic information system (GIS) may be a more fruitful approach to assessing any possible associations between unit of assignment and CCEP participation rate and health outcome. These data could provide a basis for conducting case-control studies of specific outcomes and various exposures.

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## **Potential Exposure(s)**

Veterans' concerns regarding hazardous exposures which may have occurred during the Persian Gulf War have also been a concern of clinicians who have provided health care to Gulf War veterans. The experience of combat may involve exposure to a variety of potential health hazards. These exposures could include physical, chemical, and infectious hazards, and

psycho/social stressors. However, in general, the application of engineering controls in the design of military equipment, intensive training regarding the use of personal protective measures, and adherence to safe operating procedures are intended to minimize health risks associated with military operations. Service members knowledgeable about specific exposures can provide useful information for correlation with symptoms and diagnostic findings. However, interpreting the clinical significance of these self-reported exposures must be considered within the context of available pharmacologic, toxicologic, clinical, and epidemiologic information.

Although exposure to chemical and biologic warfare (CBW) agents has been hypothesized as a possible cause of ill health, both DoD and the Defense Science Board Task Force have concluded that there is no persuasive evidence for exposure of U.S. troops to such agents.<sup>4</sup> This conclusion is based on a number of factors including the fact that no characteristic casualties were reported. A recent independent evaluation by the Institute of Medicine, National Academy of Sciences concluded: "In light of this negative evidence from highly placed sources, claims of exposure to chemical or biological warfare agents should not be made or given credence in the absence of reliable data to the contrary."<sup>23</sup>

Pyridostigmine bromide (PB) has been hypothesized to be a possible cause of chronic illness in Gulf War veterans. Troops were provided PB during the Persian Gulf War to help protect against the lethal effects of CW nerve agents.<sup>24</sup> Though this Food and Drug Administration (FDA) approved drug is not licensed for this military use, it has been approved by FDA under investigational new drug (IND) provisions. It has been used since the 1950s in anesthesia and for myasthenia gravis in doses as high as ten times those taken by troops during the Persian Gulf War, without any long-term effects. In addition, studies of this drug when taken in low doses have not revealed any serious, chronic side effects.<sup>25,26,27</sup> Whether or not pyridostigmine bromide and other chemicals such as DEET might have interactive effects at the dosage administered during the Gulf War is unclear at this time. Additional research studies are underway on this question.

Two vaccines, botulinum toxoid and anthrax, also have been postulated to be possible causes of ill health among Persian Gulf veterans. The botulinum vaccine is not believed to be a likely cause of veterans' health concerns since it has previously been used without evidence of chronic complications and was given to only 8,000 troops in the Gulf. While not licensed by the FDA for use in protecting troops against botulinum toxin, botulinum vaccine was approved for use during the Gulf War under the provision of an FDA investigational new drug. The FDA-licensed anthrax vaccine has been used for several decades without any major adverse effects.<sup>28,29</sup>

A total of 12 cases of viscerotropic leishmaniasis and 20 cases of cutaneous leishmaniasis have been diagnosed among U.S. troops.<sup>8</sup> Although difficult to diagnose, leishmania infection is not considered to be a cause of widespread illness because most troops with documented leishmaniasis have had characteristic, objective signs of disease, including elevated temperature, lymphadenopathy, hepatosplenomegaly, and skin rash.<sup>30</sup> Currently, no other infectious diseases have been demonstrated to cause chronic morbidity among a significant number of Persian Gulf veterans.<sup>31</sup>

Desert Storm troops were exposed to several potentially hazardous chemical compounds in the Gulf, most notably smoke from 605 oil well fires. However, studies conducted thus far indicate that the health risks from exposure to oil fire smoke were minimal because of the lofting of the smoke above ground level and nearly complete combustion of most chemical substances.<sup>15,32</sup>

U.S. troops were also exposed to low levels of several pesticides that are routinely used in the commercial market and by DoD. Long-term sequelae from these pesticides have been found only when exposure was very high and caused acute illness, but no acute toxicity due to pesticide exposure was reported among coalition troops during ODS/S. Nevertheless, the possibility that pyridostigmine bromide in combination with such pesticides could have acute or chronic effects is being investigated.<sup>20</sup>

Another unique, potential environmental hazard of the Gulf war was exposure to depleted uranium (DU) munitions. DU poses little health risk when external to the body. However, there may be some risk resulting from aerosolization when DU impacts on armored targets or catches

fire. There were 35 U.S. soldiers in vehicles struck by DU, and approximately 32 other U.S. soldiers were potentially exposed while fighting a fire in a munitions storage area and from servicing vehicles hit by DU munitions.<sup>4</sup> Other ground-based troops are not considered to be at risk because of the very low levels of radiation associated with DU munitions.<sup>4</sup>

Some Persian Gulf troops may have been exposed to a number of other potential environmental hazards, including microwaves; chemical-agent-resistant-coating (CARC) paint vapors containing isocyanate; various petroleum products; and airborne allergens and irritants.<sup>33</sup> At this time, none of these exposures has been identified as a primary cause of illness, because the exposures involved small numbers of troops and low concentrations of agent were involved and because there was no evidence of acute illness reported in-theater. In addition, such substances are not known to cause the types of chronic illnesses reported by Gulf War veterans.<sup>4,15,20</sup>

The Gulf War setting was quite threatening and there were many situations where participants had good reasons to be fearful. U.S. troops encountered an extremely harsh desert environment, where they were crowded into warehouses and tents with little personal privacy and few amenities. No one knew that coalition forces eventually would win a quick and decisive war. Most troops did not fight a “four-day war,” but spent months isolated in the desert, under constant stress and uncertain about their own survival and the well-being of their families.<sup>34</sup> From the outset of the deployment, active duty service members and reservists heard media reports about the devastating capabilities of Iraqi chemical and biological weapons. In anticipation of possible SCUD attacks, and in response to required training and false alarms from sensitive chemical detection devices, service members repeatedly donned cumbersome gear designed to protect them from such weapons, making life even more difficult.

In spite of these stressful conditions, Army medical evacuations for psychiatric reasons were considerably lower (2.7/1000 evacuations per year)<sup>4,35</sup> than seen in previous conflicts.<sup>36</sup> However, several months after the war, some clinicians began to report mild cases of PTSD among Gulf War veterans who did not have previous psychiatric histories.<sup>4,10,13</sup> PTSD has been previously diagnosed in other populations that have experienced a traumatic event.<sup>4,37,38,39,40,41</sup>

Although participants self-report a wide range of exposures, no objective information was available through the CCEP regarding the intensity, frequency, duration, or any routes of exposures that could further characterize actual health risks. Since exposure data generally was not collected during the Gulf War, most self-reported exposures cannot be validated or confirmed. Difficulties in interpreting self-reported data include problems involving uncertainty about the identity of hazards; inadequate information about exposure level; and recall bias (greater attention to exposures that were at the time frightening or uncomfortable, or perceived as being threats to health or life). For at least some of the potential exposures, there is independent and objective data that is discordant with CCEP participants' self-reported exposures, so that the latter may considerably overestimate actual exposure.

For example, several of the potential exposures that occurred in the Persian Gulf (as self-reported by CCEP participants) were restricted to a limited number of units involved in specialized occupations or certain geographic locations and/or to unique circumstances involving relatively small numbers of individuals. Malaria prophylaxis was provided only to selected units based upon geographic location, primarily those situated in southern Iraq, yet 22% of CCEP participants indicate they received it. With respect to DU, only approximately 30 individuals are known to have been exposed to DU fragments as a result of injuries, yet nearly 15% of CCEP participants report exposure to DU. The extent to which additional exposures to DU could have occurred is unknown. In the case of CARC paint, approximately 47% of CCEP participants report exposure, although only approximately 1000 individuals were assigned to the in-theater maintenance operations involved in the industrial application of this material. Continued analysis of the CCEP population by UIC-specific locations and military occupational specialty groups should help clarify how to interpret these self-reported exposures.

To support the latter effort, the U.S. Army Center for Health Promotion and Preventive Medicine (USACHPPM) is currently integrating exposure data sets, troop movement data, and satellite imagery of the oil well fire period into a geographic information system (GIS) model, thereby enabling spatial and temporal analyses. Additionally, information from operational, intelligence, medical sources, research databases, and anecdotal accounts of veterans is being correlated with

CCEP and GIS findings to further clarify possible relationships among troop location(s), exposures, and clinical findings among Persian Gulf veterans.

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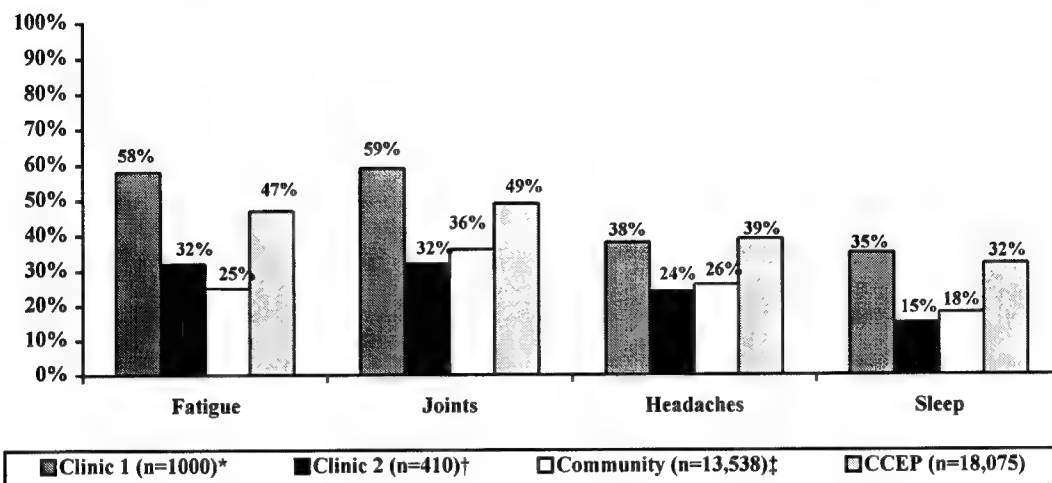
## Symptoms

CCEP participants reported a wide variety of symptoms that span various organ systems. The most commonly reported symptoms include fatigue, joint pain, headaches, rash, and sleep disturbance. The median number of reported symptoms per CCEP participant was five. As presented in previous CCEP reports, there appears to be a strong consistency in the types of reported symptoms between other large population studies of outpatient medical clinics and symptoms reported by CCEP participants. However, other large population studies of outpatient medical clinics typically include much older patients. Moreover, women are usually the majority in these community samples, since women are more likely to seek medical care than men.

Although the limited published studies of symptoms of patients in other clinical and survey settings are not fully comparable to the CCEP program, clearly these do suggest that the types of symptoms reported in the CCEP are not unique to this group.<sup>42,43,44</sup> However, comparison samples tend to average at least 20-25 years older and frequently include very elderly patients. For example, Figure 5 presents data from three community samples. Clinic 1, a study of 1000 patients who received care at four primary care clinics in the U.S., reported that 58 percent of patients reported fatigue, 59 percent reported joint pain, and 35 percent reported sleep disturbances. The comparable percentages for the CCEP are 45 percent, 49 percent, and 32 percent, respectively. However, the community sample averaged 55 years of age and ranged in age up to 91 years old. The CCEP average age was 34, and participants ranged in age up to 68. Similarly, in Clinic 2, a study of 410 patients attending a military general medicine clinic with an average age of 61.4 years, 32 percent reported fatigue, 32 percent reported joint pain, and 15 percent reported sleep disturbances. The publication describing Study 3, which includes 13,538 individuals, does not include an average age, but reports that 14.5 percent are 65 or older. This study differed from the other community studies and the CCEP in that these individuals were randomly selected from five communities and were not necessarily seeking medical care at the

time they were studied. In the third study 25% reported fatigue, 36% reported joint pain, and 18% reported sleep disturbances.

**Figure 5. Common Symptom Prevalence as Reported in Three Studies of Outpatient Practice in the United States, as Compared with CCEP**



\* Clinic Survey 1 = 1000 patients presenting for care at four primary care clinics in the U.S.

† Clinic Survey 2 = 410 patients attending a military general medicine clinic.

‡ Community Survey 3 = Random survey of 13,538 persons in four communities in the U.S.

Since fatigue, joint pain, and sleep disturbances are all associated with age, the similarities and difference between the CCEP and the community sample and military medical clinic are difficult to interpret. While clearly indication that the CCEP participants do not suffer from unique ailments, these comparisons suggest that the percentage of CCEP participants with such symptoms is unusually high, particularly for individuals of that age group. Headaches, which are less likely to be age-related, were reported by 38 percent of the participants of Clinic 1 and 39 percent of CCEP participants, but only 24 percent and 26 percent of the other two community surveys. Since headaches are a common symptom, it is important to know how this question was asked and whether the CCEP participants were reporting chronic headaches or headaches that differed in any way from those reported by the other three samples.

Patients commonly report experiencing multiple symptoms. Studies have shown that when patients complete symptom checklists, one-third of patients complain of 0-1 symptom, one-third complain of 2-3 symptoms, and one-third complain of 4 or more symptoms.<sup>43,46</sup> Research

conducted by Kroenke et al. indicates that typical outpatients will endorse a median of 4 symptoms as bothersome.<sup>44,47</sup> CCEP patients report a median of 5 symptoms per patient.

It is important to note that physical symptoms in both clinic patients and the general population frequently lack a clear-cut or definitive physical explanation or “cause.” Four community-based studies have shown that 20% to 75% of symptoms lack an association with a definitive diagnosis after a medical evaluation.<sup>42,44,46,47</sup> A reasonable estimate in general outpatient practice is that about one-third of symptoms cannot be linked to a defined diagnosis. Carefully designed studies using appropriate comparison groups will help determine whether the symptoms reported by Gulf War veterans are unique in character, frequency of occurrence, and patterns of association.

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## Diagnoses

The types of primary diagnoses commonly seen in the CCEP involve a variety of conditions such as tension headache, fatigue, depression, PTSD, nonspecific headache, migraine, joint pain, asthma, irritable colon. These primary diagnoses span all diagnostic categories of the ICD-9-CM. However, over half (65%) of all primary diagnoses fall into four diagnostic groups: psychological conditions; musculoskeletal diseases; symptoms, signs, ill-defined conditions; and healthy.

Eighty percent of CCEP participants received more than one diagnosis. About 20% of CCEP participants received a single primary diagnosis. For individuals with a primary diagnosis of respiratory; symptoms, signs, ill-defined conditions; musculoskeletal diseases; or psychological conditions a frequency distribution of secondary diagnoses indicates that the additional diagnosis is most likely to be in the same ICD-9 category as the first (primary), generally followed by musculoskeletal, psychological, or ill-defined.

## Psychological Conditions

The most frequent primary diagnostic category in the CCEP population is psychological conditions. The most frequent psychological conditions are somatoform problems, especially

tension headache; nonspecific, mild, or stress-related anxiety and/or depression; posttraumatic stress disorder; and alcohol-related disorders (Table 30).

**Table 30. Most Frequent Psychological Conditions among CCEP Participants (N=18,075)**

Psychological Condition	CCEP	
	Primary Diagnosis (%)	Any Diagnosis (%)
Somatization Disorder	0.6	1.5
Tension Headache	3.4	11.3
Mood Depression	2.9	6.2
Major Depressive Disorder	1.8	3.0
Neurotic Depression	1.1	3.0
Anxiety Disorders	0.7	2.2
Posttraumatic Stress Disorder	2.8	5.2
Adjustment Disorders	1.3	2.5
Substance Related Disorders	0.3	2.9
Alcohol Related Disorders	0.4	1.7

Psychological conditions such as depression, anxiety, and somatoform disorders are common in primary care, existing in 25-35% of all patients presenting for care in the outpatient setting.<sup>50,51</sup> However, direct comparison with the CCEP population is confounded by differences in age, gender, and ethnicity.

The prevalence of psychological conditions in CCEP participants may be increased because patients with persistent or unexplained symptoms have high rates (50% or more) of underlying mood or anxiety disorders. This need not always mean that the symptoms are caused by the mood or anxiety disorder, since it is possible that depression or anxiety can be a consequence of persistent, disabling physical symptoms. Nonetheless, the mood or anxiety disorders that coexist in half or more of such patients can further aggravate such symptoms through worsening sleep, increased fatigue, lowered pain tolerance, and mental suffering.

Patients complaining of unexplained or ill-defined physical symptoms may have coexisting conditions with associated depression and anxiety. Studies have demonstrated that ill-defined (compared with better-defined) symptoms or syndromes tend to occur much more frequently in

individuals with common, treatable anxiety and depressive disorders.<sup>50,51</sup> The severity of ill-defined symptoms associated with depression and anxiety commonly diminish in response to treatment of the underlying psychiatric condition.

## **Musculoskeletal Diseases**

The second most common primary diagnostic category within the CCEP population is musculoskeletal disease. Primary diagnoses coding within the musculoskeletal area accounted for 18% of the primary diagnoses in the CCEP. This group includes autoimmune disorders such as rheumatoid arthritis, systemic lupus erythromatosus, and Sjorgen's syndrome; degenerative disorders such as degenerative joint disease and osteoarthritis; and traumatic, disuse, or overuse inflammatory conditions such as tendonitis, bursitis, patellofemoral syndrome, and lower back pain.

Review of the CCEP population reveals that autoimmune disorders are very rare as either primary or secondary diagnoses. The most common primary diagnosis within this group is arthralgia (2.96% of all primary diagnoses) followed by degenerative joint disease/osteoarthritis (2.52%). Complaints about a specific joint (particularly the knee) are common, as are tendonitis and bursitis. These diagnoses are not inconsistent with the expected morbidity to be seen in a population of military members.

Fibromyalgia is a syndrome of unknown etiology that manifests as widespread pain with specific tender pressure points. It is associated with painful but nonarthritic joints. It is also associated with poor sleep hygiene and nonrestorative sleep. Of the CCEP participants, 1.53% have been diagnosed with fibromyalgia as either a primary or secondary diagnosis. This rate does not differ from that of the general population as a whole.<sup>52</sup>

The majority of diagnoses falling within the musculoskeletal group are wear-and-tear disorders (recurrent strains, sprains, and other chronic degenerative conditions) that should be expected in physically active military populations. There is no evidence of autoimmune disorders

precipitated by exposures in the Persian Gulf. While the musculoskeletal category is the third most commonly occurring diagnostic group, the disability of this group is not significant. Only 19.2% of the participants with a primary diagnosis in this group indicated they had missed work in the 90 days prior to their CCEP exam. Only 7% had lost seven or more days. Of the four most common categories, only "healthy" had fewer days lost.

### **Symptoms, Signs, and Ill-Defined Conditions**

The third most common diagnostic category of primary diagnosis of CCEP participants is the category of symptoms, signs, and ill-defined conditions. Approximately 18% of CCEP participants have primary diagnoses in this ICD-9-CM category. This category includes symptoms, signs, ill-defined conditions, abnormal laboratory results or other investigative abnormalities which are not elsewhere classified in the ICD-9-CM. Although an illness or symptom may fall in the 780-799 ICD-9-CM code range, that illness or symptom may very well represent a well-defined condition not classified elsewhere (such as obstructive sleep apnea or a nonspecific laboratory abnormality, e.g., elevated sediment rate). However, this ICD-9-CM category also includes patients with persistent symptoms whose physical examinations and diagnostic testing did not provide a diagnosis. Patients such as these often end up with a "symptomatic" diagnosis, e.g., malaise and fatigue, lower back pain, or headache, rather than a more precise, anatomic or pathophysiologic diagnosis.

Within the CCEP, it is apparent that many of the patients with multiple diagnoses commonly have a secondary diagnosis in the symptoms, signs, ill-defined conditions category.

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## **Characterization of Individuals with More Than One Diagnosis**

Eighty percent of CCEP participants received more than one diagnosis. In an effort to characterize, clinically, the pattern of diagnoses in some of these individuals, the frequency distribution of secondary diagnoses was examined for patients with a primary diagnosis in one of the four major diagnostic categories (psychological conditions; musculoskeletal diseases;

symptoms, signs and ill-defined conditions; or respiratory). Analysis of the frequency distribution of secondary diagnoses in this group of patients displays a rather consistent pattern involving three prominent features:

- The initial secondary diagnosis is most likely to be in the same ICD-9-CM category as the primary.
- Diagnoses involving musculoskeletal diseases; psychological conditions; and symptoms, signs, and ill-defined conditions are prominent as secondary diagnoses irrespective of the primary diagnosis.
- The proportions of other ICD-9 categories (excluding musculoskeletal diseases, psychological conditions, and symptoms, signs, and ill-defined conditions) remain relatively constant and at a relatively low level regardless of the primary diagnosis.

These observations are consistent with earlier analyses of the CCEP results, which have shown that diagnoses involving musculoskeletal diseases; psychological conditions; and symptoms, signs and ill-defined conditions are predominant conditions within the CCEP population overall. The current analysis confirms that this pattern is repeated within the major diagnostic categories as well, and shows that CCEP patients with multiple diagnoses commonly have a secondary diagnosis in the same organ system as the primary diagnosis. The latter observation seems consistent with clinical experience in that the manner in which physicians determine the rank order of diagnoses is based on the severity of the medical condition and the relative contribution of additional diagnoses to the overall clinical presentation.

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## **NAMCS Comparison**

The prominent differences that exist between the NAMCS and CCEP populations among many of the diagnostic categories may be explained when the unique characteristics of these groups are considered. Most of the military personnel within CCEP probably face markedly different

occupational experiences than most civilians found within the NAMCS population. There are also likely to be more clinical visits for acute and routine health care needs in randomly selected civilian populations like NAMCS.

CCEP participants experienced a difficult occupational experience unlike that of their civilian counterparts, e.g., deployment to the Persian Gulf region. Numerous studies have established the impacts this type of setting may have on an individual, including the development of a number of psychological symptoms and psychiatric diagnoses<sup>53,54,55</sup> and various symptoms that cannot be associated with a definitive diagnosis.<sup>56,57,58</sup> This would explain the higher percentage of psychological conditions and symptoms, signs and ill-defined conditions within the CCEP population. Psychological conditions may also be more common within the CCEP population because standardized instruments are used routinely, and use of these may increase the physician's likelihood of giving a psychological diagnosis.

Service members must maintain certain levels of physical fitness, and many are required to participate in demanding training programs, placing considerable stress on muscles and joints. These mandatory activities may account for the increased prevalence of musculoskeletal conditions in the CCEP population.

The differing reasons people seek health care may provide reasonable explanations for the higher percentages of individuals with respiratory system diagnoses in NAMCS. In most instances, people presenting to the CCEP are concerned about persistent problems. On the other hand, the randomly selected patients who visit physicians surveyed in NAMCS may present for a wide variety of reasons. For example, people may seek health care for an acute problem, one of the most common of which is an upper respiratory illness. This could account for the higher percentage of respiratory system diagnoses. Many individuals may see a health care provider for a routine or required physical examination and not have an acute condition of any kind, resulting in a relatively high percentage of people with healthy diagnoses, as seen among females in NAMCS as compared to CCEP. In previous comparisons made between NAMCS and CCEP populations, gender was not considered, and the higher percentages of genitourinary system

diagnoses within NAMCS were considered to possibly reflect the larger proportion of women in that survey.<sup>7</sup>

Standard reasons for outpatient visits in the civilian sector may also account for the higher percentage of people with diagnoses of injury and poisoning in the NAMCS population. Such patients are acutely ill or injured, come in promptly for care, and are treated within a matter of hours to a few days. Thus, these would be common in an office practice seeing acute and chronic patients, but would be rare in a sample of patients with persistent symptoms, such as the CCEP.

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## Physicians' Review

DoD physicians who are specialists in the areas of respiratory disorders, dermatology, neurology, infectious diseases, sleep disorders, and memory problems were asked to review the diagnoses in their clinical areas of expertise. The comments that follow reflect their impressions of the CCEP results within the broad context of their overall clinical experience.

### Respiratory Disorders

A primary diagnosis of a respiratory disorder was the fifth most common diagnostic category among CCEP participants, following the diagnostic categories of psychological conditions; musculoskeletal diseases; symptoms, signs, and ill-defined conditions and healthy. Non-infectious respiratory conditions were reported as 3,693 primary or secondary diagnoses in the first 17,370 CCEP participants completing their evaluation. The most common respiratory diagnosis was allergic rhinitis at 6% followed by asthma at 4.7%. Cases of sinusitis, both acute and chronic, accounted for 757 or 4.3% of the diagnoses. When reactive and obstructive airway diseases were combined, they accounted for 6.1% or 1,074 diagnoses.

Any attempt to compare these frequency distributions to other cohorts is fraught with difficulty. Most other cohorts report disease occurrence as either age-adjusted prevalence or incidence,

which was not available in this CCEP analysis. Lacking a control group (especially controlling for such factors as age, gender, ethnicity, etc.), great care must be taken in comparing CCEP participants with other populations.

Given these cautions, certain general comparisons may be made with this initial data. In the United States, the overall age-adjusted prevalence rate of self-reported asthma was 4.94%.<sup>59</sup> The non-adjusted prevalence of asthma in this CCEP analysis is 4.7%. Emphysema was reported in 15 participants in the CCEP. When combined with the diagnoses of chronic bronchitis and chronic airway obstruction, the number rose to 249, for a frequency distribution value of 6.7%. The number of cases of pulmonary fibrosis, 44, was low. Some respiratory conditions reported, e.g., deviated nasal septum (N=91) probably existed prior to and independent of service in the Gulf War. Finally, the occurrence of respiratory conditions, such as rhinitis and asthma, in a dusty environment such as exists in the Persian Gulf region may have some connection, but extensive investigation and additional data are necessary before any firm conclusion may be reached. No definitive etiology for any of these respiratory conditions reported in the CCEP may be identified based on this specific analysis.

## **Dermatologic Conditions**

The seventh most common diagnostic category among CCEP participants was dermatologic conditions. The most common dermatologic conditions in the CCEP in decreasing order were eczema/dermatitis, alopecia (predominantly common balding), folliculitis (predominantly pseudofolliculitis barbae), seborrheic dermatitis, acne, benign cysts, and xerosis/sebaceous hyperplasia.

Diseases such as malignant neoplasms of the skin may be underrepresented in the CCEP population, probably because of the young age of this population. Serious infections were also underrepresented. Psoriasis is probably underrepresented because the condition (or a history of the condition) commonly excludes persons from entry into the armed forces. Diseases such as pseudofolliculitis barbae were overrepresented because the CCEP population was a military

population consisting of male service members required to shave on a daily basis to meet military standards.

According to *Dermatology in General Medicine*, fourth edition, 1993, edited by T.B. Fitzpatrick et al., the true prevalence of skin disease is difficult to determine. This is because many dermatologic studies involve selected populations, usually patients who present with a skin complaint or who are confined to a hospital or other institution. In addition, varying social and environmental factors can influence disease occurrence or detection. The dermatologic conditions in the CCEP population closely mirror the dermatologic conditions seen in general practice.

## **Neurological Diagnoses**

The eighth most common diagnostic category of CCEP participants was neurological disorders. Headache was reported as a frequent complaint of many CCEP participants. The most common neurological diagnosis was migraine headache which accounted for 63% of the neurological diagnoses and 7.7% of all CCEP diagnoses. This prevalence was low compared to estimates in the general population. The second most common diagnosis, ulnar neuropathy or carpal tunnel syndrome, accounted for 9.5% of neurological and 1.3% of all diagnoses in CCEP.

Several other diagnoses were common in the CCEP. Benign essential tremor accounted for 2.3% of the neurological diagnosis. Nocturnal myoclonus (0.36%), narcolepsy (0.16%), and Bell's palsy (0.05%) were diagnosed in the CCEP population. Peripheral neuropathies were diagnosed in 0.25% of the CCEP population, and do not appear overrepresented. As a definitive diagnosis, multiple sclerosis (MS) was diagnosed at a frequency of 0.1%; however, if the diagnoses of possible demyelinating diseases are counted as MS, the incidence is 0.14%.

## Infectious Diseases

A primary diagnosis of an infectious disorder has been made in a very small proportion of Persian Gulf veterans examined. Of the 17,370 individuals evaluated, 392 (2.3%) received a primary diagnosis of infection with some pathogenic agent. The specific infections identified in these 392 patients varied widely. Most of these infections, 233 or 59.4%, were common dermatophytic infections. Other skin infections, such as yeast, warts, and scabies, comprised another 28 or 7.1% of the primary infectious diagnoses.

Systemic infections were reported for 131 or 33.4% individuals receiving primary infectious diagnoses. Of these, hepatitis C and/or hepatitis C infection was the most common individual diagnosis, identified in 44 or 11.2%. Giardiasis, proven or probable, was diagnosed in 13 or 3.3% and *Helicobacter pylori* infections in 7 or 1.8% of patients. In the remaining 67 patients (17.1%) with primary diagnoses of systematic infections, a wide, and apparently unrelated, variety of diagnoses were made. No other single infection was the primary diagnosis in more than five patients.

The threat to deployed military personnel posed by infectious diseases was recognized, and prepared against, from the earliest stages of Operation Desert Shield. Specific diseases observed in U.S. troops during Operations Desert Shield/Storm conformed with expectations, except that incidence was generally lower than expected. During these operations, gastrointestinal illness predominated. Attack rates ranged up to 4% per week for some units deployed early, but dropped to less than 0.5% per week when control of food sources was tightened. Limited data suggest that sexually transmitted diseases occurred at a relatively low rate. Major respiratory illnesses were rare. Insect and tick-borne illnesses, a major concern, were rarely observed in theater. Only seven cases of malaria, and only one case of West Nile fever, a mosquito-borne viral illness, were detected. No rickettsial illnesses, and no other arthropod-borne viral illnesses were identified. By October 1991, 14 cases of leishmanial disease had been diagnosed, a rate substantially lower than had been anticipated based on prewar epidemiological and historical information.

This record of infectious diseases observed during the operations themselves is relevant to current complaints of Gulf War veterans. This record suggests that overall exposure to recognized pathogens was quite low. Furthermore, it suggests that no route of infection, other than ingestion of tainted food or water, was common.

## **Sleep Disturbances**

A primary diagnosis of sleep disorder was given to 4.2% of CCEP patients. Thirty percent of the primary diagnoses within the sleep disorder category, ICD-9-CM 307.4 and 780-786.09, were diagnosed as obstructive sleep apnea (ICD-9-CM 780.57). The remainder of sleep disorder categories were evenly distributed for primary diagnosis. Within the symptoms, signs and ill-defined conditions, ICD-9-CM 780-799 code range, sleep disorders were recorded in 18.6% of the diagnoses in this category.

Many epidemiological studies concerning sleeping habits have been done since 1960 in the United States and other parts of the world. The complaint of sleep disturbance is common and is reported in these studies to range between 30% and 40%.<sup>60,61,62,63</sup>

Sleep disorders represent a recognized group of medical conditions that have been internationally classified. Also, each sleep disorder has specific medical therapies that can potentially correct that condition.<sup>60</sup> One example is obstructive sleep apnea, which is characterized by repetitive apneas during sleep as a result of an anatomical obstruction. Obstructive sleep apnea can be successfully treated by various modalities, including surgery, continuous positive airway pressure (CPAP), or weight loss.

Sleep deprivation has been shown to be associated with many health problems, including poor self-rated health, depression and anxiety, chronic medical conditions, and all-cause mortality.<sup>64</sup> Sleep deprivation has also been associated with a variety of work-related problems, including higher absenteeism, decreased job performance, and lower satisfaction.<sup>63,65</sup> In a recent sleep survey of 588 employees of a San Francisco Bay Area telecommunications firm (mean age approximately 36 years), a significantly higher frequency of physical conditions, especially

headaches, neck or back pain, muscle pain, and gastrointestinal problems, were found in those reporting sleep problems. Also noted was a higher frequency of mental health conditions (anxiety, depression) in those individuals with reported sleep disturbances.<sup>63</sup> CCEP participants share many of the physical and psychosocial complaints listed above. Sleep disorders have been actively sought by CCEP physicians and a number of sleep disorders have been diagnosed and treatments instituted. Sleep questions have also been added to the CCEP health questionnaire to help screen for sleep disorders.

## Memory Complaints

Although memory loss was recorded as the primary diagnosis in 1.7% of CCEP participants, comprehensive neuropsychological evaluations have identified no patient with evidence of an underlying neurologic etiology. All group memory scores were within the normal range for one random sample (n=165) of participants receiving neuropsychological screening with *MiroCog*<sup>66</sup> at Wilford Hall Medical Center.<sup>†</sup> There were no significant differences between patients with (n=120) and without (n=45) memory complaints on all of these measures.<sup>‡</sup>

Within the ICD-9-CM 780-799 code range (symptoms, signs and ill-defined conditions), memory dysfunction accounted for 12.3% of primary diagnoses. Most of these diagnoses appeared to be based on subjective information alone, e.g., “memory loss without cognitive deficit,” which would not normally be recorded as clinical diagnoses in medical records. This tendency to diagnose memory problems in CCEP participants despite the absence of objective data may significantly inflate the incidence of this ICD-9 category in the Gulf War veteran population.

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<sup>†</sup> MicroCog Memory Index standard score 97.35; Story Immediate Recall standard score 8.53; Story Delayed Recall standard score 8.64; Percent Retention standard score 10.19.

<sup>‡</sup> Memory Index  $f = 3.43$ ,  $p = .066$ ; Story Immediate Recall  $f = 1.6$ ,  $p = 2.08$ ; Percent Retention  $f = 1.93$ ,  $p = .166$ .

Memory complaints are associated with a number of non-neurologic medical conditions seen within the CCEP population, including sleep disorders,<sup>67</sup> chronic fatigue,<sup>68</sup> posttraumatic stress syndrome,<sup>69</sup> depression, and chronic pain. Preliminary analysis of the Wilford Hall Medical Center neuropsychological data indicates that reduced memory performance is related to higher levels of psychological maladjustment,<sup>†</sup> distress,<sup>‡</sup> and psychiatric conditions.<sup>††</sup> These represent potentially treatable causes of memory dysfunction, whereas neurologically based memory disorders are considered irreversible.

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## Disability

Severe disability measured in terms of lost workdays and/or referral to the disability evaluation system is not a major characteristic of the CCEP population as a whole. CCEP participants report a relatively low number of lost days, and this does not appear to vary with organ system involvement. Relatively few CCEP participants have undergone a disability processing action. For participants who have undergone disability processing actions, information is not readily available as to whether the medical conditions being evaluated are preexisting or are related to Persian Gulf War service. Determination of the degree to which the Physical Evaluation Board (PEB) experience reflects the overall disability experience of Persian Gulf veterans is limited by the fact that many Persian Gulf War veterans are no longer on active duty, and those that are not may represent some of the more severely disabled.

When comparing categories of diagnoses of CCEP participants who met a PEB to diagnostic categories of participants who did not, the diagnostic pattern does not appear to be different except in the categories of psychological conditions; musculoskeletal diseases; and symptoms, signs and ill-defined conditions. These three categories occur at higher frequencies relative to our overall CCEP population. Further analysis is needed to interpret these differences.

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<sup>†</sup> MMPI-2 A scale x MicroCog Memory Index,  $r = -.194, p = .003$

<sup>‡</sup> MMPI-2 F scale x MicroCog Memory Index,  $r = -.272, p = .000$

<sup>††</sup> Diagnosis x MicroCog Memory Index,  $f = 11.46, p = .0008$

Some CCEP patients with severe disability may benefit from participation in special programs that focus on rehabilitation, restoration of function, and promotion of general well-being. The DoD has established Specialized Care Centers, staffed by interdisciplinary teams, to provide such programs.

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## Reproductive Outcomes

For the 8,819 CCEP participants who responded to both the pre- and postwar reproductive outcomes questions, there were increases in self-reported infertility, miscarriages, and birth defects. The interpretation of these data is problematic for a number of reasons. For example, the frequency of self-reported birth defects among the children of just CCEP participants after the war was 2.6%. This is actually lower than what was observed when analyses were conducted using discharge diagnoses from the review of medical records when Gulf War veterans were compared with Gulf War veterans.<sup>70</sup> Several possible reasons for these inconsistencies are discussed below.

The use of self-reported pre- and postwar reproductive events does not ensure either internal or external accuracy or validity, particularly given the self-selected nature of the study population. Participation in the CCEP is voluntary, and persons deciding to participate in a clinical examination could also be expected to self-report high rates of adverse reproductive conditions. If these events occurred after the war, it is reasonable for these persons to actively participate in the CCEP. However, without a comparison group it is too early to assume any causal association between the deployment and adverse reproductive outcomes. As has been mentioned previously in this report, the CCEP and the data collection instrument were not designed for research. The questionnaire was not constructed to account for other factors that could affect the responses. For example, the question related to infertility does not ask whether the subject has been examined or diagnosed with infertility, whether unprotected (or any) intercourse was occurring, or whether the subject was trying to conceive children. Also, each of the reproductive questions is open to substantially differing interpretations by the CCEP participants. Additionally, even

though most of the reproductive questions were answered by males, the information concerned female outcomes.

The frequencies of reproductive outcomes varied among different groups, when classified by race/ethnicity, age, marital status, and branch of service. Further, there are time-dependent confounding variables, such as age and changing marital status, and intent to have children, which would likely affect the frequency of some or all reproductive events over time. The presence of these uncontrolled confounders, individually or interactively, often precludes accurate interpretation of self-reported findings.

The questionnaire design and self-selected nature of the CCEP population prevent the calculation of estimates of the prevalence or risk of any reproductive events in the population of Gulf War veterans. Well-designed epidemiologic studies, comparing events among a random sample of Gulf War veterans (including those no longer on active duty) to an appropriate group, such as military personnel who did not participate in the war, are required to determine whether there is an association between Gulf War service or experiences and the risk of adverse reproductive outcomes. Several studies have already been conducted or initiated to address the broader questions of risk of adverse reproductive outcomes.

The CCEP includes 35 children with congenital abnormalities whose parents chose to enroll them in the program. These birth defects include a wide range of conditions and are not concentrated in any single organ system or congenital syndrome. Given the self-selected population in the CCEP, other Gulf War reproductive outcome studies shed light on this issue.

Investigations by state and national public health agencies and DoD have identified no elevated rates or unusual patterns of birth defects in babies born to Gulf War veterans or their spouses. For example, one study of 23 preterm labor cases with 41 matched controls (all of whose husbands had served in the Persian Gulf during ODS/S) failed to demonstrate a significant association between Gulf War service of the husband and preterm labor in the wife.<sup>71</sup> Another study, of 54 children born to Persian Gulf veterans, conducted by the Centers for Diseases Control and Prevention (CDC), the Mississippi State Department of Health, and the Department

of Veterans Affairs found that the prevalence of birth defects, premature birth, low birth weight, and other health problems among children of Mississippi Army National Guard members appeared to be similar to that found in the general population.<sup>72</sup> In yet another study, of 41,000 live births occurring in military hospitals, researchers found that the risk of birth defects noted on medical records was no higher for either men or women who served in the Gulf War than for men or women in the military who were not Gulf War veterans, and there was no association between duration of time in the theater and the risk of birth defects.<sup>70</sup> These initial epidemiologic studies conducted to date do not indicate any association between Gulf War service and risk of adverse reproductive events.

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## **Individual and Group Response to Environmental Factors Contributing to Health Consequences Among CCEP Participants**

The medical and psychological responses individuals may have after being exposed to the stress of a war environment were noted after the Civil War and World Wars I and II.<sup>73,74,75,76,77,78</sup> A high prevalence of PTSD, depression, and substance abuse was found among veterans of the Vietnam War,<sup>79,80</sup> in addition to other personal and social difficulties.<sup>81,82</sup> In a comparison with contemporaries who did not serve in Vietnam, Vietnam veterans also reported more physical symptoms and illnesses,<sup>83</sup> and were much more likely to report a general state of poor or fair health.<sup>84</sup> When these two groups were given medical examinations, few differences were found between them. Other studies have also found a correlation between levels of PTSD symptoms and reported physical health problems;<sup>85,86</sup> however, part of this is expected due to the relation of combat injury to PTSD.

The trauma of armed conflict is not unique in causing or contributing to the development of mental health problems. Very similar findings have been found in groups following natural catastrophes, with higher rates of somatic symptoms reported in populations that have experienced disasters.<sup>87,88</sup> The correlation of PTSD with somatic complaints has been noted in these situations as well.<sup>89</sup>

Studies have found that participation in combat is a risk factor for development of PTSD and other psychiatric problems in veterans.<sup>90,91</sup> Although there were relatively few individuals exposed to combat in the Persian Gulf, there were several other psychologically stressful circumstances present. Significantly higher levels of mental health symptoms were found among deployed as compared to nondeployed personnel in a study involving Army, Navy and Marine reservists, and these symptoms seemed to be correlated with higher levels of stress exposure.<sup>10,94</sup> The handling of human remains is also very stressful and was a part of Persian Gulf experience for some service members. Previous studies have indicated the presence of psychological distress in people exposed to dead bodies following a disaster.<sup>95,96</sup> A comparison of ODS/S participants who handled remains and those who did not found significantly higher levels of intrusive and avoidance symptoms in the former.<sup>97</sup> Eight months following ODS/S, considerable psychopathology was found among a group of Army reservists who served in a war zone and performed graves registration duty.<sup>98</sup> Almost half of these troops met criteria for PTSD, which was strongly associated with evidence of depressive and substance use disorders, and a number expressed concern about somatic symptoms, including difficulty sleeping (50%), feeling nervous or tense (46%), a sense of being overly tired (42%), concentration problems (38%), general aches and pains (38%), and headaches (33%). Higher levels of psychopathology were found among reservists who did graves registration work in-theater versus in the United States.<sup>99</sup> During the Persian Gulf War, Reserve and National Guard units experienced some stressors to a higher degree than active duty members. These include minimal preparation time for deployment, family and vocational disruption, and financial distress resulting from loss of civilian employment.

Findings of Israeli researchers provide further data to indicate that the stress of the Gulf War extended beyond direct combat experiences. Moderate levels of psychological distress were found in many soldiers who were not in direct combat.<sup>100</sup> These difficulties were attributed to a combination of factors, including fear of impending missile attacks, the impression created by the news media that the population of Israel was experiencing acute distress, and a low level of trust in Army authorities.

The presence of these stressors may contribute to our understanding of the considerable percentage of the CCEP population presenting with somatic symptoms previously noted to be characteristic of individuals who have experienced high levels of trauma and natural disaster related stress.

The "environmental threat" model, which addresses community reactions to plausible threats to health, may provide additional explanations for the clinical presentations that are seen in the CCEP population.<sup>101</sup> Widespread public concern emphasized the possible health risks due to environmental exposures and their potential relationships to various health problems Persian Gulf veterans were experiencing. Thus, unexplained symptoms were first attributed to ODS/S service even before thorough medical assessment and evaluations could be performed.

When trying to understand the illnesses being experienced by Gulf War veterans, or illnesses being experienced by any group of people who have been through a traumatic experience, one of the most difficult problems is understanding the higher-than-expected rates of symptoms and illness for which there is as yet no clearly identifiable cause. As has been shown in the CCEP, Gulf War veterans are experiencing real illnesses with real consequences requiring real treatments. We are trying to understand better whether these illnesses are unusual and what the primary influences have been.

Although, there is more work to be done, the results of the CCEP have clarified our understanding of Persian Gulf illnesses by providing diagnostic information derived from extensive evaluation of Gulf War veterans presenting with a variety of symptoms. However, the CCEP does not fully explain what seem to be higher-than-expected rates of some symptoms and illnesses. There are a number of possibilities that, individually or together, deserve further exploration and will help explain what may be higher rates. One possibility is that these are not really higher-than-expected rates for this population and that a comparable population that had not served in the Gulf War would experience similar rates of symptoms and illness. Another possibility is that some of the higher-than-expected rates may result from an amplification of the rate and degree of symptoms and illness by some external influence. This possibility might be tested by examining other groups of people experiencing similar levels of trauma (e.g., natural

disasters, terrorists attacks) and by examining how and to what degree external influences (media, peer groups, families, and other information sources) impact Gulf War veterans' health. A third possibility is that some number of troops in the Gulf contracted an illness that has yet to be identified through further research, although CCEP clinical evidence to date does not support this. While beyond the scope of the CCEP, all three of these possibilities, as well as others, deserve further exploration if we are to fully understand "Persian Gulf illnesses" and initiate interventions to prevent similar illnesses in the future.

Physical and psychological symptoms and manifestations after stressful circumstances are just as real and discomfoting as those that result from physical, biological, or chemical stressors. Treatments are available which may serve to relieve many of the painful symptoms that plague some Persian Gulf veterans. In addition to providing routine care for individuals who may be experiencing some difficulties related to their experiences in ODS/S, DoD has established a Specialty Care Center for those who are suffering chronic problems that are not easily treated.

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## **Discussion of Evidence For and Against a Single, Unique Syndrome**

Much of the concern that has focused on the issue of Persian Gulf illnesses has centered around whether or not Gulf War veterans are experiencing a unique illness or syndrome. The CCEP was established primarily as a clinical program to provide health care to Gulf War veterans, rather than as a research study to resolve this question. However, the results of the CCEP, including the clinical impressions of physicians at multiple centers who have examined over 18,000 patients, corroborated by basic descriptive epidemiologic analysis, provide substantial evidence for concluding that CCEP participants have a variety of different diagnoses with overlapping clinical presentations, rather than a single, unique syndrome. The IOM-CCEP Committee recently released its final report on the CCEP and found that "There is currently no clinical evidence in the CCEP for a previously unknown, serious illness among Persian Gulf veterans. If there were a new or unique illness or syndrome among Persian Gulf veterans that could cause serious impairment in a high proportion of veterans at risk, it would probably be detectable in the population of 10,020 CCEP patients. On the other hand, if an unknown illness were mild or only

affected a small proportion of veterans at risk, it might not be detectable in a case series, no matter how large.”<sup>102</sup>

The CCEP is essentially a very large collection of cases representing primarily patients who believe they may be experiencing unusual illnesses that may be related to their Gulf War experience. Case series reports provide insight into emerging occupational and environmental illnesses and can result in clinical recognition of unusual patterns of disease, particularly when the effects are severe and readily identifiable according to clinical presentation. Clinical studies and case reports, although limited because they lack comparison populations, are nonetheless very useful for characterizing illnesses.

The majority of CCEP patients who have presented with various chief complaints (and other symptoms) such as fatigue, headache, joint pain, and sleep disturbances, have received definitive diagnoses in accordance with a diagnostic protocol which exceeds the scope of care usually provided in the primary care settings. CCEP clinicians have identified a wide range of specific diagnoses (i.e., migraine headache, depression, asthma, arthritis, hypertension). However, few if any of the conditions diagnosed to date could be considered specific for any of the many different exposures implicated as potential causes of Persian Gulf illnesses. Thus as a case series, the CCEP has identified a wide spectrum of different clinical conditions rather than any singular, homogenous diagnostic entity.

The fact that the majority of CCEP participants received more than one diagnosis as a result of their clinical evaluation deserves comment. In examining subsets of patients with multiple diagnoses whose primary diagnosis is in one of the four largest disease categories (psychological conditions, musculoskeletal diseases; symptoms, signs, and ill-defined conditions; and respiratory diseases), a rather consistent pattern emerges. These patients most commonly have their initial secondary diagnosis in the same diagnostic category as the first, or in the categories of psychological, musculoskeletal, or ill-defined. Regardless of the primary diagnosis, the distribution of other ICD-9-CM categories occurs in a narrow range at any level in the diagnostic tier. These observations suggest that there is no clinically apparent clustering of diagnoses as relates to a patient's primary ICD-9-CM categorization. Factor analyses, as part of anticipated

epidemiological research studies using sophisticated computer modeling to look at discreet diagnoses, will further characterize the clinical profile of individuals with multiple diagnoses.

Approximately 20% of CCEP patients have conditions which, for classification purposes, fall within a broad and relatively nonspecific residual coding category. These conditions do not meet clinical criteria for classification elsewhere in the ICD-9-CM coding system. These patients have a variety of different conditions that are not clinically unique, are consistent with those seen by physicians in primary care practice, and are not severely disabling. While this group of patients may have relatively nonspecific conditions for the purposes of diagnostic coding, this observation is not unusual, given that about half of all diagnoses in primary care visits do not resolve into codable diagnostic entities.<sup>103</sup>

To date, a generally accepted case definition does not exist for what has been referred to as “Gulf War Syndrome.”<sup>4,17,50</sup> While multiple physical and biologic agents have been proposed as a primary cause of Gulf War veterans’ illnesses, review of the CCEP diagnostic experience reveals relatively small numbers of the types of clinical conditions that might be expected if hazardous exposures had indeed occurred on a large scale. For example, CCEP participants have few diagnoses involving adverse drug reactions and/or immune dysfunction disorder, pneumoconioses or “dust-related” disorders or pulmonary fibrosis, peripheral neuropathy that might be associated with exposure to solvents or organophosphate-based pesticides, or kidney disease that might be a manifestation of heavy metal toxicity.

The CCEP has not identified any consistent presentation for a well-defined disease or new illness with specific physical or laboratory findings based on review of available clinical data.<sup>51,52,53</sup> Historically, clinical case series have characterized new and emerging syndromes. Legionnaire’s disease and toxic shock syndrome are good examples of illnesses that emerged with rather prominent and consistent physical and laboratory findings.<sup>57,58</sup> AIDS is another example, but the clinical presentation was more varied.<sup>59</sup> At the other end of the clinical spectrum are conditions like chronic fatigue syndrome (CFS) and fibromyalgia, which can only be defined by nonspecific symptomatology.<sup>60,61</sup> The symptom-based clinical presentation of some CCEP participants appears to overlap with CFS and fibromyalgia, but relatively few numbers of CCEP participants

meet the definitional criteria for these two conditions. However, psychological symptoms or psychiatric diagnoses are a prominent feature of all three groups.<sup>63</sup>

Somatic symptoms, with no apparent pathophysiological explanation, are commonly reported in military and civilian outpatient settings.<sup>42,104,105,106,107</sup> These somatic symptoms often coexist with well-defined disorders, particularly psychological conditions.<sup>108</sup> When compared with patients with nonsomatic disorders, patients with somatic disorder see ambulatory care providers more frequently.<sup>109,110</sup> Given these findings, it is not unusual to note a sizeable number of people in the CCEP population with ill-defined and psychological conditions.

Illnesses manifested solely by combinations of symptoms with no consistent objective findings on physical examination or positive laboratory abnormalities, and for which an adequate etiologic explanation is yet to be determined, are common in clinical practice and the general population. Such "symptom syndromes" include entities such as irritable bowel syndrome, fibromyalgia, chronic fatigue syndrome (CFS), and depression. A recent study by the Centers for Disease Control and Prevention compared the prevalence of symptoms in Persian Gulf veterans to nondeployed, Persian Gulf-era veterans.<sup>111</sup> Preliminary findings indicated that chronic symptoms, similar to those seen in CCEP participants, were reported more commonly by Persian Gulf veterans than by nondeployed, Persian Gulf-era veterans. Comprehensive medical evaluations by CDC physicians and a review of medical records for 59 Persian Gulf War veterans in the initial case series did not identify any consistent physical or laboratory abnormalities. A case-control study is currently underway to compare symptoms and illnesses in deployed and nondeployed Persian Gulf War service members.

In the CCEP, clinical review and descriptive epidemiologic data have shown relatively little evidence for a unique clinical entity. CCEP participation is not strongly associated with any single demographic category (age, sex, ethnicity, branch of service, or unit of assignment). The major diagnostic categories stratified according to age, sex, and branch of service, show no exclusive relationship to any one variable. The frequency distribution of reported exposures, symptoms, and diagnoses show no marked differences between "high" and "low" participation UICs. The small number of individuals who report lost work days suggest that the majority of

the CCEP participants are not experiencing severely disabling conditions. Determination of the degree to which the CCEP disability experience reflects the overall disability of Persian Gulf veterans is limited by the fact that many Persian Gulf War veterans have separated from the military. In the future, sophisticated statistical techniques, including cluster analysis, might identify whether or not there are previously unidentified patterns of symptoms among CCEP patients. Should an unusual pattern emerge, the clinical significance of such an observation could be further assessed by searching for abnormal physical findings and laboratory results.

In summary, the overall CCEP experience, based on clinical findings of physicians and initial descriptive epidemiologic analysis, shows no evidence for a previously unknown serious illness or syndrome among Gulf War veterans who are participants in the CCEP. However, clearly the Gulf War experience may have been a cofactor in the precipitation or aggravation of certain diagnoses, such as musculoskeletal and psychiatric conditions in some individuals. Based upon the CCEP, DoD concurs with the conclusions of the Institute of Medicine which states: "If there were a new or unique illness or syndrome that could cause serious impairment in a high portion of veterans at risk, it would probably be detectable in a population of 10,020 patients. On the other hand, if an unknown illness were mild or affected only a small proportion of veterans at risk, it might not be detectable in a cases series, no matter how large."<sup>102</sup> However, future research will be needed to determine if CCEP participants are experiencing an unusual pattern of symptoms having clinical significance.

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## Causality and Health Outcomes

Finding a definite link between an illness and its cause is often a challenge within medical practice. The process of understanding the relationship between risk factors and illness is often complex. An investigation of disease causation and work-relatedness for any set of illnesses relies on the application and integration of well-conducted epidemiologic studies, environmental monitoring, well-designed toxicologic studies, identification of risk modifiers, and consideration of contributing factors to disease. The concepts of causation may be limited by the science available to prove a solid relationship between a certain exposure and a specific health outcome.

Furthermore, there may be multiple causes of an illness; a set of causes usually involves a complex interplay of agent, environmental, and host factors. Determining a causal relationship becomes even more difficult when there is an inability to validate self-reported exposures in combination with a wide spectrum of sometimes intangible or symptom-based illnesses. However, as our understanding of the pathogenesis and epidemiology of a condition becomes known, the individual factors resulting in a disease begin to become clearer. With respect to the Persian Gulf War, it is possible to correlate some illnesses with ODS/S. For example, the cases of leishmaniasis can be attributed to the Persian Gulf environment. It was the location that brought the host to the vector of disease. Other examples of linking an exposure to an illness include musculoskeletal injuries that occurred in theater and some acute infectious diseases that resulted in upper respiratory or gastrointestinal illnesses. However, as in any clinical setting, illnesses that present with vague or mild symptoms are much more difficult to link to an event or location. It is important to note that many patients in general medical practice, not just CCEP participants, have symptoms that are not the result of a specific disease or other known pathophysiological mechanism. In the final analysis, proof of a causal relationship must be based on rigorous testing and the scientific process.

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## Research Efforts

The CCEP and the VA Persian Gulf Health Registry are providing clinical information about the types of symptoms and illnesses experienced by Gulf War veterans. However these clinical programs are not able to fully characterize the prevalence, incidence, or risk factors of disease related to ODS/S deployment. Therefore, an extensive research program has been initiated by DoD, VA, and HHS to complement the clinical registry findings.<sup>8,112</sup> Among the efforts in progress are a number of major epidemiologic studies being conducted by the Naval Health Research Center, CDC, and the VA. The Naval Health Research Center, San Diego, California (in collaboration with the VA, HHS, and the University of California), is conducting a series of epidemiologic studies of military personnel. Studies include personal interviews and physiologic testing of 750 ODS/S veterans and 1500 nondeployed Gulf-era veterans, analysis of the hospitalization records of 1.2 million service members, and review of pregnancy outcomes

among Gulf War veterans and their spouses. Initial findings from these studies were presented at the American Public Health Association (APHA) conference in October 1995, as discussed earlier in this report. The VA Environmental Epidemiology Service, Washington, DC (in collaboration with DoD and HHS), is conducting a random survey of 15,000 veterans who served in the Persian Gulf and 15,000 “control” era veterans. This mail and telephone survey is designed to describe the symptomatology experienced after Gulf service, assess the current health status of veterans and their family members, including reproductive health, and evaluate potential environmental exposures. The CDC is also conducting a study to determine the prevalence of reported symptomatology, illnesses, and exposures among Persian Gulf service members who list Iowa as their home of record.

Other ongoing research studies are assessing reproductive health, evaluating diagnostic tests for leishmaniasis infection, and studying the health effects of exposure to depleted uranium and possible interactive effects of chemical exposures. This extensive research program will provide a comprehensive evaluation of the health consequences of Persian Gulf service and will contribute to the development of programs to protect the health of military personnel during future deployments.

The information maintained in the CCEP database constitutes a large case series and was not designed to be a research study. Nevertheless, the CCEP database provides valuable descriptive information and, as such, is useful for generating hypotheses for future research. Once Privacy Act provisions ensuring the protection of individual participants have been met, the entire CCEP data set will be placed in a format that will allow access to a broad range of scientific investigators. The DoD anticipates making the CCEP data set available through the National Technical Information Service and the Defense Technical Information Center this year.

# CONCLUSIONS

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The large size of the CCEP cohort and the thoroughness of CCEP examinations provide considerable clinical insight for understanding the nature of illnesses and health complaints being experienced by this group of veterans. However, self-selection of patients, differential eligibility, recall bias, inability to validate self-reported exposures, and lack of an appropriate control group limit the generalization of these findings to other Gulf War veterans.

In general, there appear to be no unique distinguishing characteristics of CCEP participants. CCEP participants served in a large number of units during the Persian Gulf. Preliminary analysis indicates no apparent clustering of CCEP participants on the basis of unit of assignment during the Gulf War. The CCEP participant self-reported exposures span a wide range of occupational and environmental chemical and physical agents, vaccines, and medications. Confirmation of these self-reported exposures was not within the scope of the CCEP, since the primary objective of the exposure questionnaire was to assist the physician in the diagnosis of the patient's medical condition. However, in specific instances, exposures are known to have been limited to relatively small numbers of individuals (e.g., depleted uranium, malaria prophylaxis, and botulinum toxoid).

CCEP participants commonly report a variety of symptoms such as fatigue, joint pain, headache, or sleep disturbances. Review of other studies of patients with similar chronic health complaints seeking primary care in the U.S. indicate that these symptoms are routinely reported and are not unique to CCEP participants. Although the types of symptoms being experienced by CCEP participants are not unique, studies using appropriate control populations will determine whether these symptoms are associated with greater illness in subsets of Persian Gulf veterans than might be expected.

The CCEP has identified a wide range of primary diagnoses commonly seen in clinical practice (e.g., tension headache, migraine headache, fatigue, osteoarthritis, back pain, depression or stress related conditions). The majority of patients have received a primary diagnosis consistent with their chief complaint. Approximately 80% of participants have more than one diagnosis. Using standard ICD-9-CM coding criteria, 51% of the CCEP diagnoses can be categorized as psychological conditions; symptoms, signs, and ill-defined conditions; and musculoskeletal and connective tissue diseases.

Using some caution with NAMCS comparisons can provide a perspective to interpret the CCEP diagnostic experience. The data suggest that the major diagnostic categories may be over-represented in the CCEP. Potential explanations for these differences include, but are not limited to:

- Aggressive “case finding,” may have differentially attracted Persian Gulf war veterans with chronic, nonspecific symptoms;
- Overrepresentation of individuals with physical conditions (musculoskeletal injuries) associated with the intense physical demands of military service;
- Detection bias resulting from use of the structured, CCEP examination protocol to diagnose physiologic and psychological conditions that might otherwise not be evident in the course of routine, primary care; and,
- Factors directly related to the Persian Gulf War experience, such as exposure to stressful circumstances, the threat of death and injury from SCUD missile attacks, CBW threat, the harsh physical environment and living conditions, and concerns about the safety of immunizations.

Concern regarding the possible existence of “unexplained illnesses” was a major consideration in the design of the CCEP. Although CCEP physicians have not identified a unique illness or syndrome, 18% of CCEP primary diagnoses can be categorized as symptoms, signs and ill-

defined conditions according to ICD-9-CM coding criteria. Coding of a diagnosis within the category of symptoms, signs and ill-defined conditions primarily reflects limitations in diagnostic and/or coding criteria rather than an impression as to whether or not the condition can be explained. It should be noted that these diagnoses refer to a variety of conditions (well-defined conditions not classified elsewhere in the ICD-9-CM system, generalized symptoms, nonspecific findings, and abnormal laboratory tests) commonly encountered in primary care medical practice. Physical symptoms in both clinic patients and the general population frequently lack a clear-cut or discrete physical explanation or "cause."

Severe disability, measured in terms of lost workdays and/or participation in the disability evaluation system, is not a major characteristic of CCEP participants. CCEP patients with severe disability may benefit from participation in special programs that focus on rehabilitation, restoration of function, and promotion of general well-being. The DoD has established Specialized Care Centers, staffed by interdisciplinary teams, to provide such programs.

The CCEP has documented symptoms and confirmed diagnoses in over 18,000 individuals. DoD physicians have diagnosed a wide range of various medical conditions commonly seen in general medical practice rather than a single, unique syndrome. The results of the CCEP are consistent with conclusions of a National Institutes of Health Technology Assessment Workshop that among Gulf War veterans "no single disease or syndrome is apparent, but rather multiple illnesses with overlapping symptoms and causes." Results of questionnaires and personal feedback received by CCEP clinicians suggest that CCEP participants have generally been satisfied with the care they have received. DoD will continue to provide comprehensive, high-quality health care to eligible Persian Gulf veterans and will maintain an ongoing search for unique symptom and illness patterns. The Department is committed to an ongoing exchange of health information with other government agencies and Persian Gulf veterans to further understand this important issue.

The Department has implemented a comprehensive medical surveillance program for U.S. Forces deploying to Bosnia. The plan incorporates many of the "lessons learned" from the

Department's experience with the CCEP. Primary elements of the medical surveillance plan include identification of populations at risk, recognition and assessment of hazardous exposures, determination of protective measures, ensuring accurate documentation of medical events, and monitoring of health outcomes. Service members received predeployment health screening to identify individuals with acute or chronic conditions that would disqualify them for deployment. Predeployment briefings focused on anticipated infectious disease threats, prevention of occupational and environmental illness and injuries, and recognition of psychological and social stressors associated with deployment. Combat Stress Units were deployed to Bosnia in recognition of the fact that controlling combat stress is a significant factor in sustaining a healthy deployed fighting force. Emphasis is being placed on improving commanders' and units' awareness so that they will identify and report stress-related complaints and/or symptoms during the deployment. Upon return from deployment to Bosnia, service members will receive a post-deployment briefing and a medical evaluation that includes a standardized psychosocial assessment. Additionally, stress management programs will be made available to service members and their families. This surveillance plan and its related programs may serve to prevent or reduce the development of illnesses, psychosocial problems, and other adverse consequences resulting from combat and military operations involving deployments.

# APPENDIX A: RELATED DoD ACTIVITIES

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## Persian Gulf “Declassification and Investigation” Effort

The Department of Defense, in an unprecedented initiative to declassify and share with the public all possible medical, intelligence, and operational information that could have affected the health of personnel involved in the Persian Gulf War, established the Persian Gulf Investigation Team. This team consists of personnel with expertise in medicine, investigation, military intelligence, and military operations. The Investigation Team has been set up to integrate and analyze classified, declassified, and unclassified material in order to explore all reasonable or possible connections to illnesses experienced by Gulf War veterans. The team is also responsible for a toll-free hotline, 1-800-472-6719, which allows veterans an opportunity to give firsthand accounts of events or environmental exposures that they feel might be related to illnesses experienced by Gulf War veterans. The hotline also accepts theories and research on this subject from health care providers. Finally, the team coordinates with all other Department of Defense, other government, and non-governmental agencies to share information on the illnesses of these veterans. Additionally, representatives from the intelligence community, the Services, the Joint Staff and the Unified Commands are collecting and processing millions of pages of Gulf War correspondence and records. As this material is declassified, it is placed on the Internet at GulfLINK (<http://www.dtic.dla.mil:80/gulflink>) along with many other documents pertaining to the subject of illnesses in Persian Gulf War veterans. The declassification program, the GulfLINK site on the Internet, and the Investigation Team are other parts of DoD’s effort to “leave no stone unturned” in answering the many questions posed by the government, ill veterans, researchers, and the general public.

## DoD Research Efforts

The following list contains only DoD research projects that are Persian Gulf related. Integrated with DoD's research studies are numerous other studies within the Departments of Veterans Affairs and Health and Human Services. In addition to the intramural research programs currently under way within DoD, VA, and HHS, there is also an extramural research program involving Persian Gulf health-related issues that will begin by the middle of 1996. A complete listing of all Persian Gulf related research will be published by the Persian Gulf Veterans' Coordinating Board.

Project ID	Expected Completion Date	Project Title	Summary/ Information
1a-g	FY-99	Epidemiologic Studies of Morbidity Among Gulf War Veterans: A Search for Etiologic Agents and Risk Factors (A group of seven epidemiologic studies)	To characterize the prevalence of symptoms, illness, hospitalizations, infertility, and adverse reproductive outcomes among Gulf War veterans; to determine whether exposures or risk factors unique to military service in the Gulf War are associated with illness
2	4th Qtr. FY-97	Physiological and Neuro-behavioral Effects in Rodents from Exposure to Pyridostigmine, Fuels, and DEET	To evaluate the potential of a simulated PGW exposure consisting of multiple exposures, alone and in combination with an imposed psychological stressor, to induce biological effects in rats. To evaluate effects for similarities with symptoms of PGI. To determine whether the rodent model can reproduce symptoms reported in PGW veterans
4	May 1994	The General Well-Being of Gulf War Era Service Personnel from the States of Pennsylvania and Hawaii: A Survey	Assess the general sense of well-being of Gulf War era veterans in the States of Hawaii and Pennsylvania. Completed.
5	Sep 1998	Health Hazards of Operational Stress	To determine risk factors for the development of physical and psychological symptoms in response to operational stress.
7a	Sep. 1997	Health Risk Assessment of Embedded Depleted Uranium: Behavior, Physiology, Histology, and Biokinetic Modeling	To evaluate health risks associated with tissue-embedded DU fragments by studying behavioral, physiological, and histological consequences of implanted DU in a rodent model

Project ID	Expected Completion Date	Project Title	Summary/ Information
7b	Oct. 1998	Carcinogenicity of Depleted Uranium Fragments	To assess the carcinogenic risks associated with long-term exposure to DU-containing shrapnel in wounds
8a	Awaiting Funding	Serologic Diagnosis of Viscerotropic Leishmaniasis	To develop a reliable serologic test for viscerotropic leishmaniasis
8b	Awaiting Funding	Development of a <i>Leishmania</i> skin test antigen (LSTA)	To develop a reliable skin test for <i>Leishmania</i> infection
10	Mar. 1995	Acute Oral Toxicity Study involving PB, DEET, and permethrin	To determine potential toxic interactions when pyridostigmine bromide, permethrin, and DEET are given concurrently to male rats by gavage to analyze concerns about possible synergism of pyridostigmine taken by service members in ODS to protect them against potential nerve agent exposure and the insecticides permethrin and DEET, which were used by SM's in ODS. Complete.
11	FY-96	Male/Female Differential Tolerances to Pyridostigmine Bromide	To determine whether males and females have different tolerances to doctrinal dose (30 mg every 8 hrs) of pyridostigmine bromide
12	Multiple Products With Different Schedules For Each	Forward Deployable Diagnostics for Infectious Diseases	To develop a series of simple diagnostic assays suitable for forward deployed preventive medicine teams, Area Medical, and Forward Laboratories
13	1998	Effects of Persian Gulf War Service on Military Working Dogs	To test the hypothesis that there will be no differences in pathologic diagnoses between a PG MWD cohort and a matched comparison group never deployed to SWA. If hypothesis not supported, then possibility exists that differences in diagnoses between the two cohorts may be due to deployment to SWA and the dates of deployment and location in PG theater will be compared among the PG MWDs, and conceivably to those of PG veterans
14	FY-96	Risk Factors among U.S. Army Soldiers for Enrolling in the Department of Veterans Affairs Gulf War Registry	To determine the presence of unique characteristics of Army personnel enrolled in the VA Registry of Persian Gulf veterans

Project ID	Expected Completion Date	Project Title	Summary/ Information
15	Jan. 1995	Comparative Mortality among U.S. Military Personnel Worldwide During Operations Desert Shield and Desert Storm	To characterize disease and nonbattle injury mortality experience of U.S. military personnel during ODS/S. To determine whether U.S. military personnel deployed to SW Asia had a higher rate of death than U.S. military personnel who did not deploy. Completed.
16	Feb. 1994	Kuwait Oil Fire Health Risk Assessment	To characterize both the carcinogenic and noncarcinogenic health risks to DoD troops and civilian employees exposed to the environment affected by the oil fires during and after ODS. Preliminary risk assessment completed. Risk by Unit analyses ongoing.
17	May 1992	Retrospective Studies Involving Military Use of Pyridostigmine as a Pretreatment for Nerve Agent Poisoning	To obtain safety data for New Drug Application with the FDA to help perform retrospective evaluation of effects of pyridostigmine use in the Persian Gulf. Data collection ongoing.
18	Late 1996	Kuwait Oil Fires Troop Exposure Assessment Model	To respond to Public Law 102-190, section 734, by characterizing the potential carcinogenic and non-carcinogenic health risks to U.S. military personnel exposed to the environment affected by the oil well fires during and after ODS
20	July 1995	A Statistical Study Correlating the Reported Cases of Gulf War Syndrome to Battlefield Locations of Afflicted U.S. Army Personnel During the Iraq-Kuwait War, Part 1, Method to Relate Troop Deployment and the Reported Cases of Gulf War Syndrome and Probable Incidence of Maladies Defined by the International Code of Diseases ICD-9-CM	To devise a procedure for counting the collections of symptoms and diagnoses of veterans' illnesses and relating them to the U.S. military grid system locations in the Kuwait-Iraq-Saudi Arabian theater of operations
21	Dec. 1996	Possible Relationship between Multiple Chemical Sensitivity of Insect Repellent (DEET) and Carbamate (Pyridostigmine) in Gulf War Veterans' Illnesses; Study of Variability in Pyridostigmine Inhibition of Blood Cholinesterases in Healthy Adults and Individuals with Symptoms Following Participation in ODS	To determine whether symptoms exhibited by some GW veterans are due to altered pyridostigmine inhibition kinetics and/or the synergistic effect of insect repellent on pyridostigmine inhibition

Project ID	Expected Completion Date	Project Title	Summary/ Information
22	May 1998	Chronic Organophosphorus Exposure and Cognition	To evaluate the effects of low-level sub-chronic exposure to an organophosphorus cholinesterase inhibitor on normal cognitive function in animal models. LTGs are to identify underlying mechanisms of organic brain damage caused by environmental toxins and to develop treatment strategies to improve memory/cognitive performance in affected patients
23	Sep 1998	Acute and Long-Term Impact of Deployment to Southwest Asia on the Physical and Mental Health of Soldiers and Their Families	To determine the impact of deployment to SWA on the health of soldiers and their families

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# APPENDIX B: METHODS

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## Clinical Evaluation Process

All Military Health Services System (MHSS) eligible beneficiaries are eligible for the CCEP program. These include:

- Persian Gulf War veterans now on active duty or retired;
- Members on full-time Active Guard/Reserve program who are PGW veterans;
- PGW veterans who are members of the Reserve components who are placed on orders by the relevant unit or Reserve Headquarters;
- Family members (spouses, children, etc.) who are eligible for DoD health care;
- DoD civilians (current and former) if eligible in accordance with Civilian Personnel Guidance.

Participants enroll in CCEP either by calling a toll-free number (1-800-796-9699), which provides information and referrals to individuals requesting medical evaluations, or by contacting their local military medical treatment facility (MTF). The MTF commander is responsible for all aspects of the CCEP at the MTF level. Working for the MTF commander, the MTF CCEP physician is responsible for the medical issues and for ensuring that the examinations conducted are consistent with the established CCEP protocol. The MTF CCEP physician is required to be a board-certified family practitioner or specialist in internal medicine.

Developed by a multidisciplinary team of DoD and VA medical specialists, the CCEP provides a two-phase, comprehensive medical evaluation. Phase I is conducted at the local MTF and consists of a history and medical examination comparable in scope and thoroughness to an in-patient hospital admissions evaluation. The medical review includes questions about family history, health, occupation, unique exposures in the Gulf War, and a structured review of

symptoms. Health care providers specifically inquire about the symptoms and Persian Gulf exposures listed on the CCEP Provider-Administered Patient Questionnaire. The medical examination focuses on patients' symptoms and health concerns and includes standard laboratory tests (complete blood count, urinalysis, serum chemistries) and other tests as clinically indicated.

Individuals who require additional evaluation after completing the MTF-level Phase I evaluation and appropriate consultations may be referred to one of 14 Regional Medical Centers (RMCs) for Phase II evaluations. RMCs are tertiary care medical centers that have representation from most major medical disciplines. Phase II evaluations consist of symptom-specific examinations, additional laboratory tests, and specialty consultations according to the prescribed protocol.

For CCEP participants suffering from chronic, debilitating symptoms, the DoD has established a Specialized Care Center (SCC) at Walter Reed Army Medical Center (Eastern Region), and has planned a second center, currently scheduled to open in mid 1996, at Wilford Hall Medical Center (Western Region). The SCC provides additional evaluation, care, and rehabilitation through an intensive three-week evaluation and care program designed to restore participants to a maximum state of health and fitness. A multidisciplinary team of physicians from various specialties, behavioral health psychologists, nurses, and physical and occupational therapists comprise the staff of the SCCs. The treatment program is modeled after multidisciplinary pain centers, which have proven effective in treating patients with chronic, debilitating diseases.

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## **Institute of Medicine (IOM)**

The IOM, at the request of the DoD, formed a panel of experts in epidemiology, occupational medicine, internal medicine, infectious diseases, psychiatry/psychology, community mental health, allergy/immunology, and other disciplines to review the CCEP. This panel assesses the effectiveness of the CCEP and makes recommendations on the means of improving the collection and maintenance of information.

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## **Data Management Process**

The original documentation from a CCEP examination is placed into the participant's health record by the MTF conducting the examination. Each MTF maintains a copy of the evaluation record and forwards a copy to the DoD CCEP Program Management Team (PMT) in Falls Church, Virginia.

Once received by the CCEP PMT, the records are logged in and delivered to the CCEP contractor, who places the record into the CCEP automated tracking system, assigns it a tracking number, and puts the record through a quality assurance (QA) procedure. This process includes verification of completeness of the record and ensures valid diagnostic coding in accordance with International Classification of Diseases-Ninth Revision, Clinical Modification (ICD-9-CM) standards. Records failing the QA procedure are delivered to a records research team, which contacts the RMC to gather needed information and, upon receipt, returns the completed record to the QA review team.

In order to ensure database validity, personnel from the RMCs periodically visit the contractor site and perform a line-by-line verification of all complete, in-process, and deficient records for their regions. The contractor provides a daily count and a weekly total of complete records by MTF and DoD region to the CCEP PMT.

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## **Quality Control Procedures**

Data, initially entered into a relational database, were translated into a statistical package data set to be reviewed and analyzed. Missing or inconsistent data items and data outside of realistic ranges were edited as appropriate. Tests, such as gender being consistent with gender-specific diagnostic codes, were run to reveal illogical relationships among fields. Tests were run on each data field reporting the frequency of each value observed for the data field being examined.

Missing demographic data was replaced using master files from the Defense Manpower Data Center (DMDC).

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## **Analytic Approach**

### **Demographics**

CCEP participants can be divided into several categories:

- All individuals on active duty during the Gulf War,
- Reserve/Guard personnel mobilized during the Gulf War,
- Active duty, reserve, guard personnel in the Gulf War theater of operations,
- DoD civilians in the Gulf War theater of operations, and
- Family members (spouses and children) of those listed above

This report is based on 18,598 completed evaluations. The primary focus of the results section is the 18,075 military (active, guard, reserve) and civilian participants who were physically located in the theater of operations during the Persian Gulf War. The in-theater CCEP participants have been, to a close approximation, identified by use of a Unit Identification Code (UIC) assigned to each individual through a match of social security numbers with the master files maintained by the DMDC, Monterey, California. The demographics (age, sex, race, rank, service, etc.) of the in-theater 18,075 CCEP participants were compared with those of the total Gulf War military population of 696,530.

Each CCEP participant's date of birth was recorded and used to calculate age. Categorization of age into groups was carried out with ages calculated as of the start of Operation Desert Storm (August 2, 1990). Age categories were: 17 to 20 years of age, 21 to 25 years of age, 26 to 30 years of age, 31 to 35 years of age, and 36 to 65 years of age.

The CCEP data set identified the race and ethnicity of participants. Some racial minorities, such as Native Americans or Asian and Pacific Islanders, were combined into a single category of Other in the statistical data set. The race/ethnicity categories utilized are; White, Black, Hispanic and Other/Unknown (including Asians, Native Americans, and Pacific Islanders).

### **Self-Reported Exposures**

All CCEP participants who were in the theater of operations during ODS/S responded (yes, no, don't know) to a list of possible exposures, including smoke from oil fires; fumes from tent heaters; passive cigarette smoke; pyridostigmine; immunizations against anthrax or botulism; antimalarial medication; ate contaminated food, drank or bathed in contaminated water, ate non-Armed Forces food, drank non-Armed Forces water, and exposure to microwaves. These self-reported exposures were examined according to frequency of occurrence in the total CCEP data set and in various subgroups represented in the CCEP.

### **Physician-Elicited Symptoms**

In the CCEP questionnaire, the dates of onset and duration were designated for 15 specific symptoms categories. Positive responses were recorded in these fields; negative responses left these fields blank. A Yes/No category was created for each of the specified symptoms. A date of onset (Month/Year) was entered if known. In addition, a text field was entered for each subject's chief complaint. As many of these complaints as possible were assigned to 66 separate categories, including the 15 specific symptoms listed on the questionnaire.

### **Diagnoses**

Upon completion of the CCEP examination, each participant is assigned diagnoses (one primary and up to six secondary) that may include the diagnosis of "healthy" in the absence of significant medical problems. Primary diagnoses were examined for frequency of occurrence in the in-theater CCEP participants and for variations in frequency of occurrence among other categories

of individuals in the CCEP. Distributions (categorization) of diagnoses were according to the ICD-9-CM.

The ICD-9-CM is a statistical classification system that arranges the elements of morbidity reporting (clinical diagnoses) into groupings of diseases and injuries according to preestablished criteria. ICD-9-CM was published in 1977 by HHS with guidelines set by the American Hospital Association (AHA) and maintains total compatibility with the international system of ICD-9 established by the World Health Organization (WHO). It is revised and updated annually.

The format for ICD-9-CM is the classification of diseases and injuries into 17 chapters based on the multiple axes of etiology, anatomical site, and circumstances of onset. A three-digit basic code for diseases and injuries is assigned, followed by a decimal point that separates the basic code from a possible fourth-digit subcategory and a fifth-digit subclassification. The principle of hierarchy is used within this five-digit coding system, going from the more specific to the less specific. The grouping of diseases and injuries into chapters, sections, categories, and subcategories provides a workable capacity for statistical morbidity reporting and allows for the systematic tabulation, storage, and retrieval of disease-related data. ICD-9-CM has also become a standard for use by third-party payer systems for the reimbursement of health care costs.

## **Reproductive Outcomes**

Reproductive outcomes were obtained through use of a set of six pairs of questions concerning the participants' self-reported reproductive experiences prior to and after ODS/S service. These fields were used to identify members whose reproductive results had changed after ODS/S service.

## Unit Identification Codes

There were 687,851 individuals deployed to the Persian Gulf for whom unit identification data existed. These individuals were assigned to military units designated by 13,450 unique UICs. The number of deployed personnel assigned to a single UIC varied from one person to several thousand (e.g., an aircraft carrier crew). Additionally, the Air Force used a limited number of large “administrative” UICs (for example one UIC had 20,978 personnel assigned). Of the 18,075 in-theater CCEP participants with completed evaluations, 16,917 had UIC information available. These CCEP participants were assigned to 4,056 different UICs, to which 537,637 service members (77% of the total force) were assigned. It is possible that units with high levels of participation in the CCEP may represent units with different exposures during the Gulf War, or different health experiences since the war. A comparison of the exposures and outcomes may provide insight that is useful in understanding the complaints of Gulf War veterans.

Any definition of low or high CCEP participation is necessarily arbitrary, since there is no information from earlier studies to provide guidance. The approach taken in this report was to examine the distribution of participation rates and to contrast the experiences from the extremes of the distribution. In order to provide for statistical stability, units with fewer than 40 members in the Gulf theater were excluded from consideration. Because the Air Force and the Navy utilize UICs to identify very large units that may include many smaller and discrete units, all units with 1,000 or more members in the Gulf were also excluded.

The number of CCEP participants per UIC was examined. After excluding UICs with fewer than 40 members in the Gulf theater and UICs with 1,000 or more members as described earlier, the distribution of CCEP participant rates was stratified into quintiles. Because the quintile of units with highest participation had substantially more members in the CCEP (n=5074) than the lowest quintile (n=1043), the second lowest quintile (n=1331) was combined with the first. Thus, the comparisons are between the CCEP members in the highest quintile to the combined populations of the two lowest CCEP participation rate quintiles.

## **Self-Reported Lost Workdays**

CCEP participants were asked how many days of work they had lost in the 90 days prior to their medical evaluation. Responses were divided into those with no days lost and those with lost days. Individuals in these categories were compared with respect to demographic characteristics, symptoms, exposures, personal threat experience, and diagnoses.

## **Physical Evaluation Boards**

Physical Evaluation Boards (PEBs) are medical condition evaluation procedure boards accomplished within each of the services when a member develops a medical condition that may preclude the member's ability to perform his or her mission satisfactorily. This information was provided to CCEP by the four services and includes all members who have undergone a PEB since August 1990. The consolidated data set was matched by social security number against the master Persian Gulf War dataset and against the CCEP data set. A comparison of PEB rates of PGW veterans and non-PGW veterans was made and compared to CCEP participant PEB rates.

## **National Ambulatory Medical Care Survey (NAMCS)**

The NAMCS, performed by the National Center for Health Statistics, includes data from a representative sample of physician office visits.<sup>45</sup> NAMCS utilizes a multistage probability sampling design. NAMCS data were recoded to agree in format with the CCEP data set. The data fields used from the NAMCS 1990 set are Age, Sex, and the various diagnostic codes.

## **Program Satisfaction**

Upon the completion of each examination phase or upon declining to participate in the examination process, each participant is requested to answer “yes” or “no” to the following question:

“Were you satisfied with the care you received in the program?”

Additional space is available on the form for the participant to provide narrative comments should he or she desire to do so.

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## **Statistical Analysis**

Statistical analysis included measuring the mean and median of continuous variables and determining the proportion falling into certain levels (such as the proportion with seven or more days lost from work). Categorical variables were assessed in several ways. The ability to accomplish a wide range of statistical analyses (tests) is limited by the fact that the CCEP is a self-selected case series and not a research project containing norms and comparative data. The CCEP can characterize the symptoms and illnesses in PGW veterans and provide substantial clinical evidence for a general assessment of veterans’ health status subsequent to the PGW.

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# APPENDIX C: ICD-9-CM CODE DISTRIBUTION (Primary Diagnosis)

ICD-9 CM Subcategories*	ICD-9	Frequency	Percent
<b>Infectious Diseases</b>			
INTESTINAL INFECTIOUS DISEASES	(001-009)	17	0.1
TUBERCULOSIS	(010-018)	2	<.05
ZOONOTIC BACTERIAL DISEASES	(020-027)	2	<.05
OTHER BACTERIAL DISEASES	(030-041)	9	<.05
HUMAN IMMUNODEFICIENCY VIRUS (HIV) INFECTION	(042)	3	<.05
POLIOMYELITIS AND OTHER NON-ANTHROPOD-BORNE VIRAL DISEASES OF CENTRAL NERVOUS SYSTEM	(045-049)	2	<.05
VIRAL DISEASES ACCOMPANIED BY EXANTHEM	(050-057)	10	0.1
ARTHROPOD-BORNE VIRAL DISEASES	(060-067)	0	0.0
OTHER DISEASES DUE TO VIRUSES AND CHLAMYDIAE	(070-079)	85	0.5
RICKETTSIOSES AND OTHER ARTHROPOD-BORNE DISEASES	(080-088)	12	0.1
SYPHILIS AND OTHER VENEREAL DISEASES	(090-099)	6	<.05
OTHER SPIROCHETAL DISEASES	(100-105)	0	0.0
MYCOSES	(110-118)	260	1.4
HELMINTHIASES	(120-129)	1	<.05
OTHER INFECTIOUS AND PARASITIC DISEASES	(130-136)	60	0.3
LATE EFFECTS OF INFECTIOUS AND PARASITIC DISEASES	(137-139)	1	<.05
<b>TOTAL</b>		<b>470</b>	<b>2.6</b>
<b>Neoplasms</b>			
MALIGNANT NEOPLASM OF LIP, ORAL CAVITY, AND PHARYNX	(140-149)	0	0.0
MALIGNANT NEOPLASM OF DIGESTIVE ORGANS AND PERITONEUM	(150-159)	1	<.05
MALIGNANT NEOPLASM OF RESPIRATORY AND INTRATHORACIC ORGANS	(160-165)	3	<.05
MALIGNANT NEOPLASM OF BONE, CONNECTIVE TISSUE, SKIN, AND BREAST	(170-176)	11	0.1
MALIGNANT NEOPLASM OF GENITOURINARY ORGANS	(179-189)	7	<.05
MALIGNANT NEOPLASM OF OTHER AND UNSPECIFIED SITES	(190-199)	8	<.05
MALIGNANT NEOPLASM OF LYMPHATIC AND HEMATOPOIETIC TISSUE	(200-208)	22	0.1
BENIGN NEOPLASMS	(210-229)	73	0.4
CARCINOMA IN SITU	(230-234)	2	<.05
NEOPLASMS OF UNCERTAIN BEHAVIOR	(235-238)	15	0.1
NEOPLASMS OF UNSPECIFIED NATURE	(239)	2	<.05
<b>TOTAL</b>		<b>144</b>	<b>0.8</b>
<b>Endocrine, Nutritional &amp; Metabolic Disorders</b>			
DISORDERS OF THYROID GLAND	(240-246)	126	0.7
DISEASES OF OTHER ENDOCRINE GLANDS	(250-259)	81	0.4
NUTRITIONAL DEFICIENCIES	(260-269)	5	<.05
OTHER METABOLIC AND IMMUNITY DISORDERS	(270-279)	152	0.8
<b>TOTAL</b>		<b>364</b>	<b>2.0</b>

ICD-9 CM Subcategories*	ICD-9	Frequency	Percent
<b>Diseases of the Blood &amp; Blood Forming Organs</b>			
DISEASES OF THE BLOOD & BLOOD FORMING ORGANS	(280-289)	97	0.5
<b>TOTAL</b>		<b>97</b>	<b>0.5</b>
<b>Psychoses &amp; Mental Disorders</b>			
ORGANIC PSYCHOTIC CONDITIONS	(290-294)	105	0.6
OTHER PSYCHOSES	(295-299)	368	2.0
NEUROTIC DISORDERS, PERSONALITY DISORDERS, AND OTHER NONPSYCHOTIC MENTAL DISORDERS	(300-316)	2847	15.8
MENTAL RETARDATION	(317-319)	1	<.05
<b>TOTAL</b>		<b>3321</b>	<b>18.4</b>
<b>Diseases of the Nervous System &amp; Sensory Organs</b>			
INFLAMMATORY DISEASES OF THE CENTRAL NERVOUS SYSTEM	(320-326)	1	<.05
HEREDITARY AND DEGENERATIVE DISEASES OF THE CENTRAL NERVOUS SYSTEM	(330-337)	40	0.2
OTHER DISORDERS OF THE CENTRAL NERVOUS SYSTEM	(340-349)	603	3.3
DISORDERS OF THE PERIPHERAL NERVOUS SYSTEM	(350-359)	149	0.8
DISORDERS OF THE EYE AND ADNEXA	(360-379)	99	0.5
DISEASES OF THE EAR AND MASTOID PROCESS	(380-389)	137	0.8
<b>TOTAL</b>		<b>1029</b>	<b>5.7</b>
<b>Diseases of the Circulatory System</b>			
ACUTE RHEUMATIC FEVER	(390-392)	2	<.05
CHRONIC RHEUMATIC HEART DISEASE	(393-398)	1	<.05
HYPERTENSIVE DISEASE	(401-405)	194	1.1
ISCHEMIC HEART DISEASE	(410-414)	35	0.2
DISEASES OF PULMONARY CIRCULATION	(415-417)	2	<.05
OTHER FORMS OF HEART DISEASE	(420-429)	75	0.4
CEREBROVASCULAR DISEASE	(430-438)	15	0.1
DISEASES OF ARTERIES, ARTERIOLES, AND CAPILLARIES	(440-448)	29	0.2
DISEASES OF VEINS AND LYMPHATICS, AND OTHER DISEASES OF CIRCULATORY SYSTEM	(451-459)	43	0.2
<b>TOTAL</b>		<b>396</b>	<b>2.2</b>
<b>Diseases of the Respiratory System</b>			
ACUTE RESPIRATORY INFECTIONS	(460-466)	26	0.1
OTHER DISEASES OF THE UPPER RESPIRATORY TRACT	(470-478)	619	3.4
PNEUMONIA AND INFLUENZA	(480-487)	3	<.05
CHRONIC OBSTRUCTIVE PULMONARY DISEASE AND ALLIED CONDITIONS	(490-496)	506	2.8
PNEUMOCONIOSES AND OTHER LUNG DISEASES DUE TO EXTERNAL AGENTS	(500-508)	2	<.05
OTHER DISEASES OF RESPIRATORY SYSTEM	(510-519)	73	0.4
<b>TOTAL</b>		<b>1229</b>	<b>6.8</b>
<b>Diseases of the Digestive System</b>			
DISEASES OF ORAL CAVITY, SALIVARY GLANDS, AND JAW	(520-529)	58	0.3
DISEASES OF ESOPHAGUS, STOMACH, AND DUODENUM	(530-537)	472	2.6
APPENDICITIS	(540-543)	1	<.05
HERNIA OF ABDOMINAL CAVITY	(550-553)	22	0.1

ICD-9 CM Subcategories*	ICD-9	Frequency	Percent
NONINFECTIOUS ENTERITIS AND COLITIS	(555-558)	187	1.0
OTHER DISEASES OF INTESTINES AND PERITONEUM	(560-569)	337	1.9
OTHER DISEASES OF DIGESTIVE SYSTEM	(570-579)	54	0.3
<b>TOTAL</b>		<b>1131</b>	<b>6.3</b>
<b>Diseases of the Genitourinary System</b>			
NEPHRITIS, NEPHROTIC SYNDROME, AND NEPHROSIS	(580-589)	12	0.1
OTHER DISEASES OF URINARY SYSTEM	(590-599)	65	0.4
DISEASES OF MALE GENITAL ORGANS	(600-608)	95	0.5
DISORDERS OF BREASTS	(610-611)	7	<.05
INFLAMMATORY DISEASES OF FEMALE PELVIC ORGANS	(614-616)	4	<.05
OTHER DISORDERS OF FEMALE GENITAL TRACT	(617-629)	50	0.3
<b>TOTAL</b>		<b>233</b>	<b>1.3</b>
<b>Complications of Pregnancy &amp; Childbirth</b>			
ECTOPIC AND MOLAR PREGNANCY	(630-633)	0	0.0
OTHER PREGNANCY WITH ABORTIVE OUTCOME	(634-639)	1	<.05
COMPLICATIONS MAINLY RELATED TO PREGNANCY	(640-648)	2	<.05
NORMAL DELIVERY, AND OTHER INDICATIONS FOR CARE IN PREGNANCY, LABOR, AND DELIVERY	(650-659)	0	0.0
COMPLICATIONS OCCURRING MAINLY IN THE COURSE OF LABOR AND DELIVERY	(660-669)	0	0.0
COMPLICATIONS OF THE PUERPERIUM	(670-676)	0	0.0
LATE EFFECT OF COMPLICATION OF PREGNANCY, CHILDBIRTH, AND THE PUERPERIUM (NON-SPEC DX)	(677-677)	0	0.0
<b>TOTAL</b>		<b>3</b>	<b>&lt;.05</b>
<b>Diseases of Skin &amp; Subcutaneous Tissue</b>			
INFECTIONS OF SKIN AND SUBCUTANEOUS TISSUE	(680-686)	17	0.1
OTHER INFLAMMATORY CONDITIONS OF SKIN AND SUBCUTANEOUS TISSUE	(690-698)	513	2.8
OTHER DISEASES OF SKIN AND SUBCUTANEOUS TISSUE	(700-709)	595	3.3
<b>TOTAL</b>		<b>1125</b>	<b>6.2</b>
<b>Diseases of the Musculoskeletal System</b>			
ARTHROPATHIES AND RELATED DISORDERS	(710-719)	1860	10.3
DORSOPATHIES	(720-724)	680	3.8
RHEUMATISM, EXCLUDING THE BACK	(725-729)	658	3.6
OSTEOPATHIES, CHONDROPATHIES, AND ACQUIRED MUSCULOSKELETAL DEFORMITIES	(730-739)	109	0.6
<b>TOTAL</b>		<b>3307</b>	<b>18.3</b>
<b>Congenital Anomalies</b>			
CONGENITAL ANOMALIES	(740-759)	39	0.2
MATERNAL CAUSES OF PERINATAL MORBIDITY AND MORTALITY	(760-763)	0	0.0
<b>TOTAL</b>		<b>39</b>	<b>0.2</b>
<b>Perinatal Conditions</b>			
OTHER CONDITIONS ORIGINATING IN THE PERINATAL PERIOD	(764-779)	2	<.05
<b>TOTAL</b>		<b>2</b>	<b>&lt;.05</b>

ICD-9 CM Subcategories*	ICD-9	Frequency	Percent
<b>Symptoms, Signs &amp; Ill-Defined Conditions</b>			
SYMPTOMS	(780-789)	3125	17.3
NONSPECIFIC ABNORMAL FINDINGS	(790-796)	103	0.6
ILL-DEFINED AND UNKNOWN CAUSES OF MORBIDITY AND MORTALITY	(797-799)	11	0.1
<b>TOTAL</b>		<b>3239</b>	<b>17.9</b>
<b>Injury &amp; Poisoning</b>			
FRACTURE OF SKULL	(800-804)	0	0.0
FRACTURE OF NECK AND TRUNK	(805-809)	1	<.05
FRACTURE OF UPPER LIMBS	(810-819)	2	<.05
FRACTURE OF LOWER LIMBS	(820-829)	3	<.05
DISLOCATION	(830-839)	10	0.1
SPRAINS AND STRAINS OF JOINTS AND ADJACENT MUSCLES	(840-848)	81	0.4
INTRACRANIAL INJURY, EXCLUDING THOSE WITH SKULL FRACTURE	(850-854)	0	0.0
INTERNAL INJURY OF CHEST, ABDOMEN, AND PELVIS	(860-869)	1	<.05
OPEN WOUND OF HEAD, NECK, AND TRUNK	(870-879)	0	0.0
OPEN WOUND OF UPPER LIMB	(880-887)	1	<.05
OPEN WOUND OF LOWER LIMB	(890-897)	0	0.0
INJURY TO BLOOD VESSELS	(900-904)	0	0.0
LATE EFFECTS OF INJURIES, POISONINGS, TOXIC EFFECTS, AND OTHER EXTERNAL CAUSES	(905-909)	5	<.05
SUPERFICIAL INJURY	(910-919)	4	<.05
CONTUSION WITH INTACT SKIN SURFACE	(920-924)	0	0.0
CRUSHING INJURY	(925-929)	0	0.0
EFFECTS OF FOREIGN BODY ENTERING THROUGH ORIFICE	(930-939)	0	0.0
BURNS	(940-949)	0	0.0
INJURY TO NERVES AND SPINAL CORD	(950-957)	2	<.05
CERTAIN TRAUMATIC COMPLICATIONS AND UNSPECIFIED INJURIES	(958-959)	7	<.05
POISONING BY DRUGS, MEDICINAL, AND BIOLOGICAL SUBSTANCES	(960-979)	0	0.0
TOXIC EFFECTS OF SUBSTANCES CHIEFLY NONMEDICINAL AS TO SOURCES	(980-989)	1	<.05
OTHER AND UNSPECIFIED EFFECTS OF EXTERNAL CAUSES	(990-995)	21	0.1
COMPLICATIONS OF SURGICAL AND MEDICAL CARE, NOT ELSEWHERE CLASSIFIED	(996-999)	2	<.05
<b>TOTAL</b>		<b>141</b>	<b>0.8</b>
<b>Supplementary Factors</b>			
HIV POSITIVE, NOT OTHERWISE SPECIFIED	(V08.0)	1	<.05
HISTORY OF MALIGNANT NEOPLASM OF THYROID	(V10.87)	1	<.05
HISTORY OF NEUROSIS	(V11.2)	1	<.05
HISTORY OF INFECTIOUS AND PARASITIC DISEASES	(V12.0)	6	<.05
HISTORY OF DISEASES OF BLOOD AND BLOOD FORMING ORGANS	(V12.3)	3	<.05
HISTORY OF DISEASES OF RESPIRATORY SYSTEM	(V12.6)	1	<.05
HISTORY OF DISEASES OF SKIN AND SUBCUTANEOUS TISSUE	(V13.3)	1	<.05
HISTORY OF OTHER MUSCULOSKELETAL DISORDERS	(V13.5)	1	<.05
NORMAL PREGNANCY	(V22.2)	3	<.05

ICD-9 CM Subcategories*	ICD-9	Frequency	Percent
UNSPECIFIED MENTAL OR BEHAVIORAL PROBLEMS	(V40.9)	1	<.05
MARITAL PROBLEMS	(V61.1)	5	<.05
OTHER OCCUPATIONAL CIRCUMSTANCES OR MALADJUSTMENT	(V62.2)	4	<.05
INTERPERSONAL PROBLEMS, NOT ELSEWHERE CLASSIFIED	(V62.81)	1	<.05
OTHER PSYCHOLOGICAL OR PHYSICAL STRESS, NOT ELSEWHERE CLASSIFIED	(V62.89)	3	<.05
PERSON WITH FEARED COMPLAINT IN WHOM NO DIAGNOSIS WAS MADE	(V65.5)	1762	9.7
LACK OF PHYSICAL EXERCISE	(V69.0)	1	<.05
OBSERVATION FOR OTHER SUSPECTED MENTAL CONDITIONS	(V71.09)	1	<.05
OBSERVATION FOR OTHER SPECIFIED SUSPECTED CONDITIONS	(V71.8)	8	<.05
OBSERVATION FOR UNSPECIFIED SUSPECTED CONDITIONS	(V71.9)	1	<.05
<b>TOTAL</b>		<b>1805</b>	<b>10.0</b>
<b>TABLE TOTAL</b>		<b>18,075</b>	<b>100</b>

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# APPENDIX D: GLOSSARY OF ACRONYMS

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<b>APHA</b>	American Public Health Association
<b>CARC</b>	Chemical Agent Resistant Coating
<b>CBW</b>	Chemical and Biological Warfare
<b>CCEP</b>	Comprehensive Clinical Evaluation Program
<b>CW</b>	Chemical Warfare
<b>DNBI</b>	Disease Non-Battle Injury
<b>DoD</b>	Department of Defense
<b>DSB</b>	Defense Science Board
<b>DU</b>	Depleted Uranium
<b>FDA</b>	Food and Drug Administration
<b>HHS</b>	Department of Health and Human Services
<b>IOM</b>	Institute of Medicine
<b>MHSS</b>	Military Health Services System
<b>MTF</b>	Medical Treatment Facility
<b>NAMCS</b>	National Ambulatory Medical Care Survey
<b>NIH</b>	National Institutes of Health
<b>ODS/S</b>	Operations Desert Storm/Shield
<b>PGW</b>	Persian Gulf War
<b>PMT</b>	Program Management Team
<b>PTSD</b>	Posttraumatic Stress Disorder
<b>RMC</b>	Regional Medical Center

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<b>SCC</b>	Specialized Care Center
<b>UIC</b>	Unit Identification Code
<b>USUHS</b>	Uniformed Services University of the Health Sciences
<b>VA</b>	Department of Veterans Affairs

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